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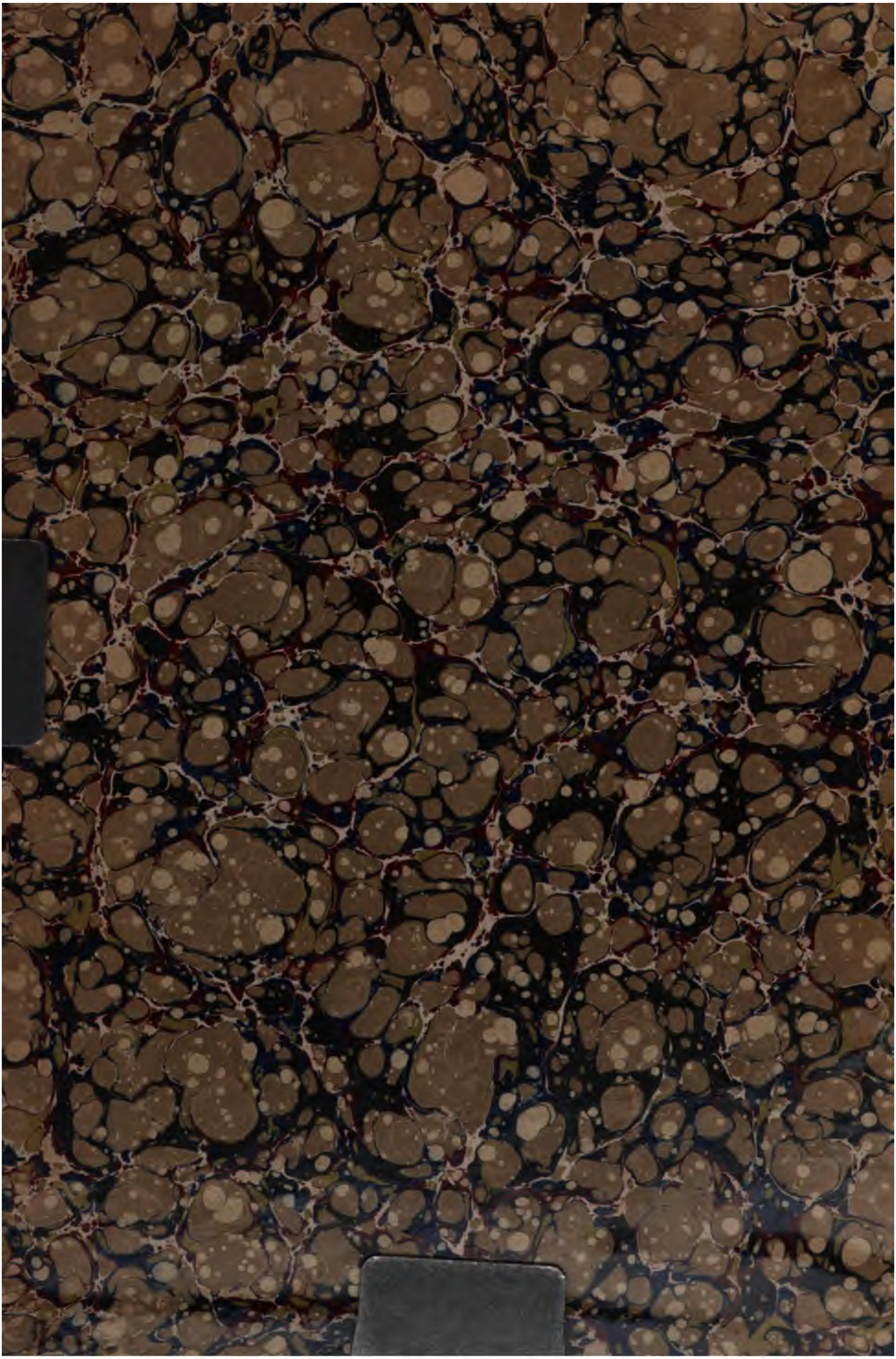

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THE PHILIPPINE

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B. MEDICAL SCIENCES

VOL. III JANUARY, 1908 No. 1

A COMPARATIVE STUDY OF TSUTSUGAMUSHI DISEASE AND SPOTTED OR TICK FEVER OF MONTANA.

By P. M. ASHBURN [1] and CHARLES F. CRAIG.[1]

I. Synonymy.
II. Introduction.
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I. SYNONYMY.

Tsutsugamushi disease; Japanese river fever; flood fever; island fever; *kedani* disease; *aka mushi* disease; *shima mushi* disease; *yochubio; shashitsu.*

Mushi is a Japanese word meaning bug, and the compounds ending with it all relate to the etiology of the disease. *Tsutsugamushi* is the term employed by most Japanese people and professional men and, as it has the prestige derived from ancient and specific usage, it will be employed in this paper.

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[1] Captain and assistant surgeon, United States Army, and first lieutenant and assistant surgeon, United States Army, constituting the United States Army Board for the Study of Tropical Diseases, as they occur in the Philippine Islands.

Spotted fever of Montana; Rocky Mountain fever; tick fever; *Pyroplasmosis hominis* (Wilson and Chowing); tick fever of the Rocky Mountains; Rocky Mountain spotted fever.

As so-called spotted fever has been described as occurring in various districts of the Rocky Mountain region, and as it has not been determined that the same infection is identical in all those parts, the term *spotted or tick fever of Montana* will be used in this paper, the disease referred to being that occurring in western Montana, particularly in the Bitter Root Valley, in Missoula and Ravalli Counties.

II. INTRODUCTION.

For many years *kedani* or *tsutsugamushi* disease has been an annual subject of the most active and painstaking investigation on the part of Japanese physicians and the Japanese Government.

One of the leading investigators of late years is Dr. M. Miyajima of the Institute for Researches of Infectious Diseases, of Tokyo. Dr. Miyajima had read of the work of Wilson and Chowning, Anderson, Stiles and others on the study of "spotted" or "tick fever" in Montana and as he had found so many points of similarity in the two diseases, he thought it quite possible that they were the same. Consequently, when he came to Manila as a representative of his Government to the Philippine Islands Medical Association, he was desirous that we should visit Japan at the proper season and determine, if possible, whether or not such is the case. Thanks to the representations of Dr. Miyajima and the liberal view taken of the matter by Major-General Leonard Wood, the Acting Surgeon-General and the War Department, we were ordered to Japan; and this report is based on the observations concerning *tsutsugamushi* disease made on that trip and those of one us (Ashburn) in 1904 and 1905 on the cases of spotted fever occurring during those years in the Bitter Root Valley in Montana.

The specific point we were to endeavor to determine, and which we think we have determined, was the question of the identity or nonidentity of the two diseases and the greater amount of emphasis will be laid on that point in this report.

However, as both diseases are so closely restricted in their locality, and so are necessarily unknown to the very great majority of medical men, a brief account of each will be given and an effort will be made to place them side by side, so that the resemblances and differences may be brought out more strikingly. The descriptions to be given are based on personal observations of some twenty-two cases of "spotted fever" and seven cases of *tsutsugamushi* disease, as well as on the writings of others who have studied one disease or the other more carefully than we could.

Both infections are still subjects of earnest and careful investigation by expert workers, and it is therefore unnecessary, and it would be futile, in a paper of this kind, to attempt the thorough consideration of them which they deserve and will receive later.

III. HISTORY OF THE TWO DISEASES.

According to Tanaka the name *tsutsugamushi* has been known since the earliest historical times, while the designation *shashitsu* occurs in Chinese writings more than a thousand years old. A quotation from one of these indicates that at the time the disease was recognized as a distinct affection and was ascribed to the bite of a mite, which occurred in summer time in certain districts which had been flooded by the spring rains. The bite was described and the statement made that after three days a high fever developed and a pustule appeared at the site of the injury. It was also recognized that only certain regions of the country harbored the infection and that the disease only appeared in persons entering them.

Tsutsugamushi was brought to the attention of the Western World by Palm in 1878 and by Bälz in 1879, and since that time it has been the subject of much painstaking work by Japanese medical men. Numerous articles have appeared in Japanese journals and a certain number of European ones; many microörganisms, including cocci, bacilli and protozoa, have been described as the cause of the disease, and several investigators are working at the present time, each with what he considers to be the causative factor. It can not be said that any one of these workers has as yet established his claim. Three hypotheses at present divide those actively engaged in the study of the disease and rule the work of investigation:

1. That the disease is caused by a bacterium, a belief favored by the workers of the Institute for Infectious Diseases.
2. That it is a protozoäl infection. Professor Ogata is the leading exponent of this idea.
3. Tanaka thinks it is due to a toxin contained in the body of the red mite.

Spotted fever of Montana has been recognized for only a few years, twenty-five at the most, while the literature relating to it has practically all been written since 1902. Wilson and Chowning in 1902 published their first account of the fever and gave their ideas as to its cause and the method of its transmission in a preliminary report to the Montana State board of health, which appeared in the Journal of the American Medical Association. It is true that Major Wood, in 1896, and Maxey in 1899 had reported a similar, or the same disease in Idaho, but the form occurring in the latter territory presents such points of difference, particularly in regard to mortality, that it is not considered in this paper.

The disease, since the work of Wilson and Chowning in 1902, has each year been the subject of careful investigation and report, and the prospects now are that its etiology will soon be well understood.

The total number of cases occurring each year is small and this fact, considered in connection with the further ones that the disease is encountered in such a limited and relatively isolated region and has been known for so short a time, makes it remarkable that the present knowledge concerning it should be as great as it is.

IV. ETIOLOGY.

Tsutsugamushi disease occurs along certain limited parts of the banks of a few rivers on the west coast of the main island of Nippon, being limited to Echigo and Akita Provinces. The distribution of the infected areas is irregular and, up to the present time, unexplainable. They are all subject to submergence by floods which occur in June, but not all flooded districts are infected, nor does the relative location of an infected district, up or down stream, seem to influence a noninfected one. The floods usually occur in June and last but a few days. Immediately after their subsidence the infective regions are not dangerous, but after a few weeks or a month and synchronously with the appearance of the *akamushi* or red mite, they become so, and any person entering them takes a considerable risk of contracting the disease. Consequently, these regions are avoided at this time by all whose poverty does not drive them there to work. As a general rule no right of ownership is exercised over such land and the very poor do, therefore, cultivate hemp on it in some places and in other parts visit it to gather mulberry leaves to feed silkworms. In either case they are apt to be bitten by red mites and it is customary for them to search carefully for their bites after leaving the places where they are encountered. However, the mites are so small as to be very difficult of detection and if the bite does not cause pain, it is frequently overlooked. Not all mites are infective and many bites therefore cause no trouble. However, a certain proportion of them do, the point bitten becoming an eschar and later an ulcer. The neighboring lymphatic glands become enlarged and painful and an attack of fever succeeds.

It is the experience of practically all who have carefully studied the disease, and they are numerous, that *every* case of it is preceded by the bite of a mite, and in the great majority of instances this is located by an examination of the region drained by the lymphatic glands, which first become enlarged and tender. So far as could be learned in Japan, Bälz's contention that such is not the case has not received support, and later investigators agree that the above method is the sole means of infection. The mite in question is the larval form of a *Trombidium,* species unknown. The larva bears a great resemblance to that of *Leptus autumnalis.* It is so small as to be almost invisible to the naked eye, it is bright red or orange in color and is found on land that has been submerged by flood. Here it is best collected by tying a monkey out over night or by catching the field mice (*Arvicola hatanedzumi* Sasaki) occurring in such regions. The insects collect in groups on or about the eyelids of the monkey, while they are always found attached in large numbers to the inner surfaces of the ears of the mice. Mites resembling these in size and color occur in many parts of Japan, but they do not attack persons. The *akamushi* of other than infected regions do not transmit disease.

Several supposed causative organisms have been described for the infection, the latest and probably the one calculated to excite most interest being Ogata's plasmodium. None of these alleged discoveries has been confirmed, and judging from what we heard and such blood examinations as we could make in Japan, it appears that Ogata's plasmodium does not exist. The causative organism is as yet unknown.

Spotted or tick fever of Montana, as known by Wilson and Chowning, Anderson, Stiles, Ricketts and Ashburn, also occurs in very strictly limited areas, particularly in a strip of country about 4 to 10 miles wide and 50 miles long, lying on the west side of the Bitter Root River and the eastern side of the Bitter Root Mountains and partly on the slopes of the latter. The country in question has a considerable fall of snow which remains on the mountains until mid June and on the highest peaks for two or three weeks longer. The Bitter Root River is largely fed from this snow and, as it begins to melt in March and continues to do so with increasing rapidity until most of it has disappeared, the stream is in a state of freshet during this time and does not again reach "low water" until July. During the same period ticks (*Dermacenter occidentalis*), which before and after these freshets are infrequently seen, appear in great numbers, particularly in the forests, thickets and uncultivated regions, and they are very apt to get on any person or animal going into such parts. Cases of "spotted" or "tick fever" likewise, and as rule, appear during the same period, and in almost all instances of infection a history of a recent visit to, or residence in, the infected district, and in many cases an account of tick bites received there, is given. Wilson and Chowning identified the tick as the carrier of the disease as early as 1902. Ashburn, after a study of all the cases occurring in 1904 and most of those in 1905, came to the conclusion that a considerable proportion of these cases gave neither history nor signs of tick bite and, for that and other reasons which it is not necessary to detail here, agreed with Stiles that the tick was not concerned in transmitting the disease. However, the more recent and very excellent work of Ricketts and of King, and their apparent success in transmitting the infection to monkeys and guinea pigs by means of the tick, seem to indicate that Wilson and Chowning were right in their belief as to the method of transmission. It may therefore be said that the disease is introduced by the bite of *D. occidentalis.* The location of the bite can not always be determined, possibly because the first symptoms of the fever do not indicate its position as is the case with *tsutsugamushi* disease. Certainly, an ulcer and lymphadenitis do not always follow. Ricketts's recent observation that nymphal ticks may transmit the disease and his suggestion that larvæ may do so, possibly accounts for the absence of a history of tick bite in some cases, as the lesion resulting from the bite of larvæ may be so insignificant as possibly to leave no trace after a few hours or a day and the larva itself may be overlooked. The majority of persons in the infected regions carefully watch and examine themselves for tick bites, and it is improbably that the bite of the adult tick is often overlooked. In nearly all cases the disease is contracted on the hill sides or "bench," high above the river, and some persons long resident in the region say that the bottom lands and islands which are subject to submersion are free from danger. Wilson and Chowning named the disease *Piroplasmosis hominis.* Later investigations, except that of Anderson, have failed to confirm their view and the disease is not now considered a piroplasmosis. The causative organism is not known.

A consideration of the etiology of the two diseases shows many points of resemblance, but also some important differences. Both occur in small and usually strictly limited areas along certain streams running through mountainous country. The district in each instance is subject to heavy snowfull in winter and the streams to spring or summer floods. Along each infected stream the dangerous spots are usually more or less uncultivated and the soil overgrown with underbrush, trees or weeds, while the immune spots are well cultivated. In each country the disease is attributed to the bite of an *Acarina*, and in each a supposed protozoön blood parasite has been described as its cause, but has not been confirmed as such. Contagion is unknown in either disease.

The differences in the etiology of the two infections are equally well marked. The *Acarina*, the bite of which causes *tsutsugamushi*, is always a six-legged, larval *Trombidium*, the adult form being unknown. The insect conveying "spotted or tick fever" of Montana is always *Dermacentor occidentalis*, and usually the adult. *Tsutsugamushi* disease always occurs *after* floods, being contracted on ground which has actually been submerged by the swollen river. Fields immediately adjoining the infected areas and but a few feet higher are considered safe. The Montana disease may precede the flooding of the streams or, more usually, accompanies it. It is very commonly contracted on ground which has not been submerged, but which is on hillsides high above the level of the river. The cases begin in March and rarely appear after the middle of July; *tsutsugamushi* disease beings to appear in July and continues to occur until some time in October.

Spotted-fever regions are uncultivated either because of the elevation and roughness of the land and the difficulty of irrigating it, or of the relative newness of the country. Regions infected with *tsutsugamushi* disease are uncultivated because of their low and flat positions, which subject them to annual floods which destroy most crops, and because, for an immemorial period, they have been recognized as dangerous.

V. SYMPTOMS.

Tsutsugamushi disease is not usually preceded by well-marked prodromata. Occasionally there may be a few days of malaise and indisposition, but its common history is that in from five to twelve days, reraly less than five, after the receipt of a bite from a red mite the patient has a chill; headache and fever follow and a group of lymphatic glands, usually those of one axilla or groin, are found to be enlarged, painful and tender. Examination of the region drained by these glands leads to the discovery of the lesion resulting from the bite. This lesion is small, circular and usually 2 to 4 millimeters in diameter. Some writers state that in its early stages the lesion is a small vesicle. In most instances it is a black or brown area of necrosis of the derma. The dark necrotic skin is very adherent, but after a varying number of days it loosens and is cast off, leaving a circular, punched-out ulcer of slightly greater diameter. The periphery of the ulcer is pinkish in color, slightly infiltrated and generally it is not painful or tender. Enlargement of the lymph vessels connecting the lesion and the large and painful glands can not be detected. The glands, while enlarged and inflamed, do not present great swelling, are not fused together, and are movable beneath the skin.

The temperature at this early stage ordinarily runs from 38°.2 C. (101° F.) to 29°.6 C. (103° F.). Tanaka states that it may reach its maximum in twenty-four hours. The pulse is from 80 to 100 and strong.

The conjunctival vessels are often injected, slight cough may be present, the tongue is moist and somewhat coated, the bowels constipated, and slight or moderate splenic enlargement demonstrable. The urine may contain albumen and the diazo-reaction is present. The patient ordinarily feels comfortable, if headache be excepted and the appetite may be surprisingly good.

As the disease advances, the above symptoms become more marked. General, slight enlargement of superficial glands occurs, the temperature reaches 40° C. (104° F. to 40°.5 C. (105° F.) and is continuous. The pulse weakens and quickens and it may become dicrotic; the first heart sound may be impure. The presence of albumen and the diazo-reaction in the urine are more marked and casts may be numerous; injection of the conjunctivæ and lachrymation are more evident; respiration is accelerated, the breath sounds are harsh, cough increases and may be harassing, although the expectoration is scanty. The entire surface of the body is apt to be hypersensitive and this condition causes complaint. Constipation usually persists, but exceptionally diarrhœa and abdominal pain and tenderness occur. The tongue becomes dry, brown in the center and glazed at the tip and edges, sordes collect and the gums may become spongy and bleed. In such cases the breath is particularly foul. Partial deafness occurs, the patient becomes stuporous and may pass into coma before death. At some period of the disease, usually from the fifth to the seventh day, although it may be a little earlier or later, an exanthem appears, first on the face and later on the chest, the forearms, the legs and the rest of the trunk; occasionally the palate and buccal surfaces also show it. The eruption consists of irregular, rather faint, dusky or pink macules or flattened papules 2 to 5 millimeters in diameter, which may become confluent on the cheeks and give an appearance of swelling. On the relatively dark skin of a Japanese, this eruption is not well shown, and on parts of the body other than the face the lesions bear a great resemblance to flea bites, with which they may be confused. They fade on pressure, but at once return when it is removed. The eruption does not itch and its duration usually is from four to seven days, although at times this period may be more or less. The eruption never becomes hæmorrhagic or petechial. Tanaka states that in rare instances it may become vesicular or pustular, but this condition is probably less frequent than his implication would lead one to believe. The period of exanthem marks the height of the disease and as the eruption begins to fade, usually about the end of the second week, the fever lessens and in a few days the temperature reaches the normal, while the general condition also rapidly improves. The patient then speedily recovers, although the little ulcer resulting from the bite may be long in healing.

The above description gives the symptoms of a case of average severity which recovers; in more severe ones which recover, the fever may last longer and the symptoms be very marked. In severer cases still, death may result on from the ninth to the fifteenth day. On the other hand, very light infection may show but slight and ephemeral fever, very trifling or no exanthem, and may not be bedfast. Nevertheless, the ulcer and lymphatic enlargement are always present and the former may be larger than usual, having a diameter of as much as 1 centimeter. The duration of the disease is usually about three weeks. It may be as long as a month or as short as one week. Parotitis, melæna and mania have been noted as complications, while coma, cardiac weakness and pulmonary œdema may be terminal features.

Spotted or *tick fever,* as it occurs in the Bitter Root Valley, begins in from one to eight days after the tick bite, in cases where the history of bite is obtainable. As in *tsutsugamushi* disease, prodromata are unusual, the sickness commonly commencing with a chill. There is not the constant signal symptom of localized lymphadenitis which enables one to find the tick bite, and when it is present it is usually due to pyogenic or other infection of the wound, and lymphangitis may accompany it, while the margins of the lesion are more inflamed and indurated than in the other disease. In many cases no tick bite can be located. When found it does not present the constant appearance of a small, round necrotic area succeed by an ulcer as in the case of the mite bite. The temperature in spotted fever is not essentially different from that in *tsutsugamushi* disease, although it does not show the constancy of type shown by the latter; the eye symptoms, constipation and splenic enlargement may be the same.

As spotted fever progresses the symptoms in the main bear a great resemblance to those of *tsutsugamushi* disease, with the following exceptions:

a. The fever in the latter disease is more typically continuous; in the former more irregular.

b. The pulse rate in spotted fever as compared with the temperature is apt to be relatively high; in *tsutsugamushi* disease it may be the opposite.

c. The majority of spotted-fever patients are dead before the end of the second week.

d. As a rule, the exanthem in spotted fever appears earlier than that of *tsutsugamushi* disease. It shows first on the wrists and ankles and rapidly spreads to cover the entire body. It is much more abundant and more plainly visible than that of *tsutsugamushi* disease, although the latter fact is doubtless related in part to the darker color of the skin in Japanese. It usually consists of macules or petechiæ, although it may resemble the rash of measles or of rötheln; but in practically all cases it soon becomes petechial or hæmorrhagic, and large extravasions may be produced by the confluence of neighboring hæmorrhagic spots. Instead of disappearing in from four to seven days this eruption usually persists until after the patient has died or recovered and slightly pigmented stains may mark its location for weeks on the bodies of persons recovering. Some of the points of extravasation may pass on to gangrene and sloughing, a thing unknown in *tsutsugamushi* disease.

e. Hæmorrhagic extravasation not infrequently takes place into the scrotal tissues of make subjects of spotted fever, never in cases of the other disease.

f. The tongue and lips of the spotted-fever case may be dry, cracked and bleeding, but the gums do not become spongy and do not ooze blood, as is sometimes the case in *tsutsugamushi* disease.

g. Parotitis, malæna and mania have not been noted as complications.

IV. BLOOD EXAMINATION.

So far as we know, no complete studies have been made of the condition of the blood in *tsutsugamushi* disease. Tanaka states that the red cells usually run from 4,800,000 to 5,200,000, the leucocytes from 6,000 to 8,000, and the hæmoglobin from 40 to 75 per cent.

On the other hand, Dr. Miyajima informed us that the red cells fall during the course of the disease to 3,000,000 or 4,000,000, while the hæmoglobin is reduced proportionately, and he also states that leucopenia obtains. He had not made differential counts of white cells. We were disappointed in not having apparatus for making blood counts and were forced to content ourselves with examinations of fresh and stained films. From such examinations we judge that the red cells are not deformed, that they stain normally, and that the differential white cell count is probably not of much assistance in diagnosis. There is apparently a well-marked leucopenia.

The number of cases examined by us is too small to enable us to draw any general conclusion as to the value of differential counts in the prognosis, but if they indicate anything, it is that they have such value.

It will be noticed that Case 4, discharged recovered, and Case 5, suffering from a third attack and apparently not very sick, both had low polymorphonuclear and high lymphocyte counts; while Cases 1 and 2, both ending fatally, and 3 and 6, both serious, if not fatal, did not show either. So far, then, as a general deduction might be drawn from the consideration of differential counts on six cases, it would appear that a relative decrease of polymorphonuclear and increase of mononuclear cells, particularly of lymphocytes, constitute a favorable prognostic omen. We were unable to recognize parasites in either fresh or stained specimens of blood, except one body in a fresh film from Case 6. The body was intracellular, amœboid, unpigmented and about 1μ in diameter. We believed it to be a young tertian parasite. (Malaria is common in the district.)

The following table shows the results of our differential counts. They are all made on blood drawn August 2, and in each case at least 400 white cells were counted.

TABLE I.—*Differential blood counts in tsutsugamushi disease.*

	Case 1, fatal.	Case 2, fatal.	Case 3, severe.	Case 6, severe.	Case 4, mild.	Case 5, mild.
Small lymphocytes	7	5	8	8	18	18
Large lymphocytes	11	10	7	12	21	27
Polymorphonuclears	74	80	84	77	54	45
Transitional and large mononuclears	8	5	1	3	6	9
Eosinophiles					1	1

In spotted fever, as in *tsutsugamushi* disease, the blood condition has not been studied sufficiently to permit the drawing of general deductions. Wilson and Chowning and Anderson agreed that the red cell counts were reduced about 20 per cent; the hæmoglobin somewhat more; while the leucocytes were increased. In one fatal case, in a pregnant woman, Ashburn found a leucocyte count of 15,600. Not enough differential counts have been made to enable us to form an opinion as to their value in prognosis. Anderson reports such a count in a recovering case, the percentages being as follows: Small lymphocytes, 9.9; large lymphocytes, 10.6; polymorphonuclears, 78.7; eosinophiles, 0.3.

Wilson and Chowning and Anderson described what they considered a *Piroplasma* in the blood of spotted-fever cases. Later observers have not confirmed this and we do not think that any organism can be seen.

VII. MORTALITY.

The mortality in *tsutsugamushi* disease has been variously estimated at from 15 to 70 per cent or more. Statistics of 567 cases carefully recorded by Dr. Miyajima give an average mortality of 27 per cent. The rate shows a steady and progressive increase from 12.5 per cent in the first decade of life to 57 in the seventh.

The mortality statistics of tick fever are not based on such a large number of cases and it is probable that many of these which are included in Wilson and Chowning's tables, but which occurred prior to 1902, were not really spotted fever. These authors nevertheless figure the percentage of mortality as 75, and that is approximately correct. This disease is therefore more fatal than the other. So far as the statistics at hand give any indication, the mortality does not steadily increase with the age of the patients.

VIII. IMMUNITY CONFERRED BY ATTACK.

One attack of *tsutsugamushi* disease does not confer permanent immunity against another. Probably a temporary immunity is always produced, but second and third attacks in later years are not rare. One of the cases seen by us in August was suffering from his third attack. As a rule, the later attacks of the disease are milder than the first.

In tick fever second and third attacks are unknown and it seems probable that they do not occur. However, the number of living persons who have had the disease is so small as to make generalizations on this point dangerous. Ricketts says that active immunity of at least two or three months' duration is produced in the monkey or guinea pig by an attack of the disease.

IX. SUSCEPTIBILITY OF ANIMALS.

Ogata states that *tsutsugamushi* disease is inoculable into kittens, apes, mice and guinea pigs. Dr. Miyajima, who has done much work on the subject, maintains that it can be produced in monkeys either by mite bite or inoculation from a patient, but not in mice or guinea pigs. Infected monkeys show fever, but not the skin or genital involvement described by Ricketts as occurring in the same class of animals inoculated with spotted fever. Wilson and Chowning thought rabbits and spermophiles to be inoculable with spotted fever; Stiles and Ashburn were unable to produce the disease in them. Ricketts and King have conveyed the infection to monkeys and guinea pigs, and more recently Ricketts appears to have produced it in the horse.

X. PROGNOSIS.

The prognosis, in view of the mortality, is considerably better in *tsutsugamushi* disease than in spotted fever, and this is particularly true with regard to young subjects. However, in neither disease can much reliance be placed on mild symptoms during the early days of sickness, for in both it too frequently happens that a patient who for some days has had very moderate fever, a good appetite, no pain, and has appeared only slightly or not at all sick, will take a turn for the worse and in a short time be in a very dangerous condition. Later, the patient may die in spite of the fair promise of the early symptoms. Prognosis, therefore, should be guarded. In both diseases pregnant women are liable to abort and die. Judging from the cases here reported, we may hope that the differential leucocyte count will prove valuable in estimating the prognosis in given cases of *tsutsugamushi* disease.

IX. PATHOLOGIC ANATOMY.

The knowledge of the conditions found *postmortem* in both diseases is as yet incomplete, because in the region of flood fever, as in that of spotted fever, there is a sentiment against autopsies and very few of them have been obtained. The only pathologic conditions recognized as characteristic of *tsutsugamushi* disease are the ulcer at the site of the bite, and the moderate lymphatic and splenic enlargement. Œdema of the lungs and hypostatic congestions may be found. The kidneys are swollen and congested and may show acute nephritis.

The findings in tick fever are not greatly different from those given above. The characteristic ulcer and the lymphatic enlargement are not present, whereas the skin lesions are striking and may include large areas of extravasation, or small patches of gangrene. Ricketts's findings of lymphatic enlargement in animals dead of experimental spotted fever indicate that more careful search might reveal such enlargement in human subjects of the disease.

XII. DIAGNOSIS.

Tsutsugamushi disease presents points of resemblance to malaria, typhoid, typhus, pneumonia, and plague; its locality and the season at which the disease occurs are of course important points of differentiation. Examination of the blood for malarial parasites and for the Widal reaction will be of further assistance, as will the absence of most of the physical signs of pneumonia and the presence of the mite bite, the lymphatic enlargement and the eruption. The character of the epidemic and the presence of plague bacilli in the sputum, glands or viscera would distinguish the disease from plague. A mild case of typhus occurring in the endemic region at the proper season would possibly be very hard to differentiate. The darker, more profuse and petechial eruption, the absence of characteristic lymphatic enlargement and of the bite and the contagiousness should make the diagnosis reasonably certain.

Spotted or tick fever of Montana bears a much closer resemblance to typhus and, in our opinion, can only be distinguished from it by its seasonal and geographical limitations and its lack of contagiousness. Spotted fever may also present a great resemblance to cerebro-spinal meningitis, from which, in the most nervous cases, it can be differentiated by consideration of season and locality, the more ephemeral nature of the nervous symptoms, the absence of such serious signs as blindness, and the occurrence of other and less nervous cases. Finally, it can be diagnosed by the autopsy. Malaria, with the exception of recurrences of the disease contracted elsewhere, does not occur in the spotted-fever country. Typhoid can be excluded by the blood examination and by the appearance of the rash.

While the wide geographical separation of the two diseases renders it improbable that anyone else will be called upon to differentiate between *tsutsugamushi* disease and tick fever of Montana, it is germane to the subject of this paper here to summarize the points of differentiation by means of parallel tables.

TSUTSUGAMUSHI DISEASE.	SPOTTED FEVER.
Geographical distribution:	
Confined to Echigo and Akita Provinces in Japan.	Confined to parts of the Rocky Mountain region.
Contracted on ground that actually has been submerged.	Contracted on ground that has not been submerged.
Season:	
First of March to end of June (usually).	End of June to October.
Etiology:	
Due to bite of infected larval *Trombidium*.	Due to bite of infected *Dermacentor occidentalis*.
Incubation:	
Five to twelve days (usually).	One to eight days.
Symptoms, early:	
Onset. Usually by chill, followed by headache, malaise.	Same. Headache and backache more common.
Pain and swelling of lymphatic glands on first or second day leads to discovery of bite.	Not so. Tick bite, if present, may be inflamed.
Bite always present and demonstrable. Shows small black area of necrosis.	Not so. When present it is usually a red mark.

TSUTSUGAMUSHI DISEASE—continued.	SPOTTED FEVER—continued.
Symptoms, early—Continued.	
Superficial lymphatic glands become enlarged elsewhere than near wound.	Not so.
Temperature 38°.3 C. (101° F.) to 39°.5 C. (103° F.).	Not so constant.
Injection of conjunctivæ and photophobia are frequent.	Same.
Nose and *throat* normal.	Sore throat occasional.
Tongue moist, slightly coated.	Same.
Constipation.	Often present, but not as a rule.
Spleen enlarged.	Same.
Symptoms, later:	
Fever to 40° C. (104° F.) or 40°.5 C. (105° F.), continuous.	More irregular and may be higher or lower.
Pulse may be slow, but is usually rapid and weak. May be dicrotic.	Almost always rapid and weak. May be dicrotic.
Exanthem usually fourth to seventh day. First on face and temples.	Usually second to fifth day. Usually first on wrists and ankles.
Indistinct or absent on thighs and arms.	Not so.
Macules or papules, dusky.	Macules or petechiæ.
Usually lasts four to seven days.	Fades more slowly.
Does not become hæmorrhagic.	Becomes hæmorrhagic.
Frequently shows in mouth.	Not so.
Hyperesthesia common through disease.	Often present.
Partial deafness frequent.	Less frequent.
Tongue and lips may crack and bleed.	Same.
Gums spongy, may ooze blood.	Not so.
Cough may be severe and paroxysmal, expectoration tenacious.	Cough common, and œdema of lungs common at end.
Perspiration common.	Not noted. Skin often dusky or marbled.
Remission at end of second week.	No constancy. Most patients dead before that.
Ulcers may be long in healing and glands remain tender.	No such condition.
Complications:	
Parotitis, malæna, mania.	Not noted.
Coma, cardiac weakness, pulmonary œdema.	Frequent.
Mortality:	
30 per cent. Increases steadily with age.	75 per cent. No steady increase with age.
Pathological anatomy:	
Ulcers, lymphadenitis, large spleen, hypostatic congestions. May be nephritis.	No ulcers. Lymphadenitis not noted. Large spleen; hypostatic congestions. May be nephritis.
Immunity:	
Not conferred by attack.	Probably conferred by one attack.

XIII. PROPHYLAXIS.

The only prophylactic measure which as yet has been put to any general use against either disease is avoidance of the infected regions. This is much easier in the case of *tsutsugamushi* disease than in that of spotted fever, because the dangerous regions are so much smaller and are plainly marked off by the very flooding that makes them dangerous, and moreover they are not residence sites. Some of the Japanese investigators are recommending that persons who are compelled to enter the dangerous regions should wear clothing saturated with petroleum. The use of carbolic baths, benzine, oil of peppermint and balsam of Peru are also advocated. The effectiveness and applicability of these measures remain to be proved. It is stated that cultivation of the soil and the use of human fæces as manure will free an infected area from the disease in about three years, if its submersion meanwhile is prevented.

XIV. TREATMENT.

So far as personal observation enables us to form opinions on this subject, it indicates that the treatment in both diseases is divisible into two classes:

1. Expectant-symptomatic.
2. Hoped-for specifics, which are apt to be the result of guesswork or of reasoning from false premises or erroneous observations.

The clinical symptoms of both diseases and the results of practice in clinically similar diseases, such as typhoid and typhus, indicate that each offers a field for a more extended use of hydrotherapy than either has yet received.

XV. CASE HISTORIES OF TSUTSUGAMUSHI DISEASE.

The following are such histories and notes as could be obtained in regard to the cases of *tsutsugamushi* disease seen by us this year:

CASE 1.—*S. Igarashi; male; age, 17 years; farmer.*

Family history.—Negative as regards *tsutsugamushi* disease.

Personal history.—Patient had been in the infected locality at various times and does not know when he was bitten by mites. This is his first attack of the disease.

Present illness.—The disease began on July 24, 1907, with a chill. The next day the patient entered the hospital. At that time the glands of one axilla were enlarged and tender, and examination of the region drained by them showed the small ulcers resulting from three bites. There was no skin eruption and the spleen was not demonstrable. The pulse was strong, frequent and regular, appetite decreased and the bowels constipated. Urine was normal. The temperature is shown by Chart 1.

On July 26 an eruption of rose-colored macules appeared on the face. Later it gradually spread over the body and limbs. The diazo-reaction was well marked in the urine of July 28, and the pulse was that day dicrotic. The eruption showed on the hard palate and the fauces, and some cough was present.

August 1: The present condition is indicated by the foregoing notes, there having been no change.

August 2: The patient is sluggish and stupid. The eruption is still present but is not prominent; the eyes are injected and suffused, the spleen is tender but not palpable; respiration is rapid and the pulse feeble. The patient sleeps well and has had no delirium.

August 3: The urine contains considerable albumen and numerous coarsely granular casts. The patient sleeps much and perspires freely, the pulse is 85 but very weak, the heart sounds feeble. There is no cough; breath sounds everywhere harsh. The eruption still shows on the face and chest, but is fading. The eyes are much injected. The tongue is dry, white in the center, glazed at the margins, the papillæ prominent; gums spongy; spleen tender, but not palpable.

August 4: The general appearance and condition are about as yesterday. The gums are very spongy and are bleeding. Cough is present and produces a scant, tenacious sputum, much discolored with blood from the gums. Respiration is rapid and somewhat irregular, the breath sounds harsh. The pulse is rapid, irregular and of low tension, the first heart sound feeble. There is slight œdema of the feet. The eruption remaining on the face is papular and the apex of each papule shows a minute scab; the conjunctivæ are much injected.

August 7: Dr. Craig and I left on the 5th to visit another infected region and on our return this morning we learn that the patient became progressively worse and died on the morning of August 6 with high temperature and œdema of the lungs. Autopsy was not obtainable.

CASE II.—*I. Hasigawa; female; age, 13 years.*

Family history.—Negative as regards this disease.

Personal history.—The patient has been in the *tsutsugamushi* infected region and was bitten by a red mite on July 17, 1907. This is her first attack of the disease.

Present illnes.—On July 22 she had a chill and next day entered the hospital. At that time she had fever, a flushed face, weak and rapid pulse, poor appetite, and diarrhœa, the last a very unusual symptom. The left femoral glands were enlarged, painful and tender and just below them was the small ulcer resulting from the mite bite. It was surrounded by a slightly infiltrated, pink border.

On July 27 the spleen was demonstrably enlarged and the urine gave the diazo reaction. It contained no albumen. The patient was delirious at times and was extremely hypersensitive. The temperature is shown by Chart 2.

August 1: Eruption appeared this morning for the first time, showing on the face. It is rubeolar in appearance, but scanty. Diarrhœa has ceased under treatment. The pulse is growing weaker. Cough is present, but unproductive of aught save pain, breath sounds everywhere harsh.

August 2: The patient slept well last night and is not delirious. The pulse is rapid and feeble; cough persists and causes abdominal pain; hyperæsthesia is very marked, and pain causes the patient often to moan. The abdomen is particularly painful and tender, but is not distended or rigid. The bowels are loose. There is a dusky, faint, scattered, macular eruption on the face, arms and legs. Tenacious mucus in the throat excites cough and nausea.

August 3: Face dusky, eyes congested, eruption less distinct; tongue dry and glazed and its papillæ prominent. Hyperæsthesia, abdominal pain and diarrhœa persist. Patient slept poorly last night and is delirious. Respiration rapid and moaning; breath sounds harsh; cough less severe and distressing. Pulse recorded as 85, but during examination it was 140 and weak. Heart sounds rapid and weak, but clear.

August 4: The patient died at 6 a. m. to-day. Delirium had ceased, but diarrhœa persisted and the heart became rapid and weaker until death occurred. Autopsy was not obtainable.

CASE III.—*H. Itagake; male; age, 14 years.*

Family history.—Negative as regards this disease.

Personal history.—The patient has visited the infected regions and was bitten by a mite on July 19. This is his first attack of *tsutsugamushi* disease.

Present illness.—The disease began with a slight chill on July 27. Since that time the patient has had moderate fever and enlargement of the lymphatic glands, particularly of the right axilla, but has felt comfortable and has not appeared to be very ill. The temperature is shown by Chart 3.

August 1: The patient has had no symptoms except the fever, slight headache and constipation, and does not appear or feel very ill. There is no eruption and the spleen is not demonstrably enlarged. The right axillary glands are swollen and tender and the skin of the same axilla shows a small ulcer with pinkish, slightly indurated and tender margins.

August 2: Face clear and bright. No eruption present and the patient appears well. The tongue is white, slightly dry and tooth-marked. The pulse is of good strength.

August 3: The face is flushed, the eyes injected, a faint eruption present. The patient appears worse than he did yesterday, but does not complain. The tongue is moist and has a white coating, the spleen somewhat enlarged and tender, but not palpable. There is no cough, but the breath sounds are harsh, especially at the apices of the lungs. The urine shows a trace of albumen and very numerous, coarsely granular casts and small round epithelium, but no blood. Examination of the fæces shows *Ascaris* eggs, but is otherwise negative.

August 4: The skin is hot, the face flushed, eyes injected, expression somnolent. The tongue is somewhat dry, red at the margins, and has a thick, yellowish white, central coat. The gums are normal. Cough is present, but there is no expectoration. Respiration is rapid and regular, the breath sounds harsh. The pulse is rapid, compressible and regular; the first sound of the heart roughened over the base and apex.

August 7: On our return to the hospital we learned that the patient had grown worse and had become very nervous, and that he had left the hospital on August 6. His subsequent history is unknown to us.

CASE IV.—*S. Asai; male; age, 17 years.*

Family history.—Negative as regards this disease.

Personal history.—Patient has been in the infected regions, but was not aware that he had been bitten by mites. On July 27 he felt listless and feverish and on the 29th he came to the hospital. At that time he had fever (see Chart 4), his face was flushed and he complained of headache and pain in the pharynx. The lymphatic glands in the left axilla were swollen and painful and careful examination revealed the presence of two small ulcers, one in the left axilla and one back of the hair line of the left frontal region.

August 1: Condition as at time of admission. No eruption has shown and the patient looks and feels well. Spleen not palpable or tender. Slight systolic roughening is noticed over base and apex of the heart. There is slight enlargement of the superficial lymphatic glands, more marked in the left axilla. Physical examination is otherwise negative.

August 2: The patient looks and feels well, has a good appetite, no pain, no eruption, and sleeps well. The ulcer on the head has healed.

August 3: The patient looks and feels well. The systolic roughening persists unchanged.

August 4: Discharged from hospital, recovered.

CASE V.—*T. Suzuki; male; farmer; age, 44 years.*

Family history.—One son had this disease two years ago.

Personal history.—The patient had an attack of *tsutsugamushi* disease at the age of 17 years and a second one at the age of 25 years. Lately he has visited the infected region, but he does not know when he was bitten by a mite. On July 28 he began to suffer from malaise and he came to the hospital on the 30th. At that time he had fever (see Chart 5) and the right inguinal glands were enlarged, painful and tender. At the right margin of the umbilicus was a very small ulcer with red, puffy edges and covered with a thin crust. There were no other symptoms.

August 1: Enlargement of the epitrochlear glands is noticed, but they are not tender. Patient feels well and appears so. Physical examination is negative.

August 2: There has been no change since yesterday. The spleen is not demonstrably enlarged, the tongue is moist, clean at the edges, and shows a white, central coat; there is no eruption; the bowels are sluggish.

August 3: There is no change in the general appearance or condition.

August 4: There is no marked change. The patient eats and sleeps well, and, except for his fever, the ulcer at the umbilicus and the lymphatic enlargement, appears to be well. The bowels are moving naturally.

August 5: The patient to-day insisted on leaving the hospital, and did so notwithstanding the persistence of fever and the remonstrances of his attendants. The subsequent history of the case is unknown to us.

CASE VI.—*Male; age, 8 years.*

Family history.—The patient's mother had *tsutsugamushi* disease twelve and his father two years ago, both recovering. An employee living in the same house also had it at one time, but the date is unknown.

Personal history.—The patient has at times been fishing in the infected region, but does not know of having received any bite from a red mite. On July 30 he had a chill and since that time has had fever.

August 2: The patient was this morning brought to hospital for the first time by his father. He has a temperature of 39°.5 C. (103°.2 F.) and severe headache. The post auricular and upper cervical glands of the left side are enlarged, tender and painful. Examination shows a mite bite just to the left of the sagittal suture at the vertex. It is a small, brown circle of necrotic skin, about 2 millimeters in diameter. The brown, necrotic tissue is loose at the margins, but most intimately adherent by its under surface to the sound scalp. The tongue has a white coat, through which the papillæ project red and prominent. The eyes are not red or inflamed. Scattered over the face is a slight eruption, which first appeared last night. It is most prominent on the cheeks and consists of faint, dusky macules, 2 to 5 millimeters in diameter, which fade on pressure and return very promptly when the pressure is relieved. The spots present the slightest perceptible degree of elevation. There is no eruption in the mouth or throat. The spleen is enlarged, the appetite poor, the bowels constipated; there is no cough and the heart and lungs are normal. Removal of the necrotic area of the bite by means of forceps and scissors leaves a small ulcer with steep margins and a whitish or grayish lining, the appearance of which is said to be very characteristic.

August 7: The patient did not enter the hospital and we have seen him but the one time. We are told that his fever is high and his condition serious. The subsequent history is unknown to us.

CASE VII.—*Sakuma; male; farmer; age, 20 years.*

Family history is negative as regards *tsutsugamushi* disease.

Personal history.—The patient has not had this disease previously. On July 27 he was bitten by a red mite. On August 3 he was taken sick with fever and a feeling of uneasiness. He continued feverish, but had no great discomfort, nor any marked symptoms, and came to the hospital on August 5. The maximum temperature that day was 40° C. (104° F.), the highest pulse rate 94. On August 6 the highest temperature was 39°.5 C. (103°.2 F.), the highest pulse rate 107.

August 7: We saw the patient for the first time this morning. He has a temperature of 39° C. (102°.2 F.), and a good pulse of 95. There is slight enlargement of the superficial lymphatic glands, most marked in the left axilla, where they are also tender. The bite is located in the left axilla and is an ulcer with a mass of black, necrotic tissue still attached to its central part. It is larger than usual, being about 1 by 0.5 centimeter. The conjunctivæ are congested, the tongue moist and white and an eruption is present this morning for the first time. This is most marked on the right cheek and consists of six dusky, very slightly elevated papules which fade on pressure. The bowels are regular and the patient has neither cough nor pain. He sleeps and eats well, but his expression is somewhat dull and listless. The spleen is slightly enlarged, but neither tender nor palpable. The examination of heart and lungs is negative.

We did not see this patient again and know nothing of his subsequent history.

XVI. CONCLUSION AS TO THE NONIDENTITY OF THE TWO DISEASES.

We think that a consideration of the facts concerning the two diseases, as at present known and set forth above, justifies the opinion that they are separate and distinct disease entities. They present many points of resemblance, but those are not sufficient to overbalance those of difference.

XVII. DOES TSUTSUGAMUSHI DISEASE OCCUR IN THE PHILIPPINE ISLANDS?

The ready answer which the large majority of medical men in the Islands would give to the above question would be in the negative and it is probable that they are correct. Nevertheless, certain cases are seen which should lead to a more complete investigation of the subject. In these Islands there occur a great many cases of anomalous fevers and these are probably of several kinds. In our report for the quarter ending June 30, 1906, we made passing reference to two which were seen by one of us at Camp Connell, Samar, in the preceding February and we are in possession of the temperature charts and the notes made on them by First Lieut. Earl H. Bruns, assistant surgeon, United States

Army. These cases bear considerable resemblance to those of *tsutsugamushi* disease and therefore it seems advisable to refer to them again and more at length.

Before discussing them it is well to mention the climatic conditions under which they occurred. Camp Connell is located on the west coast of Samar and lies but a few feet above sea level. At one side is a low, flat stretch of land that was formerly a swamp, but it has been drained and made into a target range. In time of very heavy rains water still covers the range and it may be submerged for two or three days at a time, or such was the condition in 1905 and 1906. The ordinary annual rainfall at the post is about 330 to 400 centimeters, and almost all of the precipitation occurs between the first of June and the first of January. During January the target range generally becomes dry and hard. In 1905 the post suffered from drought, which began in January and was not fully relieved until late in May. In 1906 there was again very little or no rain in January and a repetition of the condition of the previous year was feared at the time that these cases occurred. The condition of the target range in December, January and February is somewhat similar to that of the *tsutsugamushi* infected regions in Japan in June, July and August.

One of us (Ashburn) happened to be at Camp Connell investigating the question of water supply in February, 1906, and was asked to see the two cases to be quoted, because of their resemblance to the spotted fever of Montana. The notes to follow were made by Lieutenant Bruns eighteen months before we saw any sufferers from *tsutsugamushi* disease or considered the possible relationship between the two infections.

CASE A.—*D. L. C.; age, 29; private, Company M, Twenty-first Infantry.*

Family history.—Negative.

Personal history.—The patient has had the usual diseases of childhood, pneumonia at 9 years and at 14 years of age, dysentery in 1901, malaria in 1901, gonorrhœa and chancroids in 1905.

Present illness.—January 29, 1906: For the past six days he has had headache and pain in the back and has been feverish and constipated, but has had no chill. He was admitted to the hospital this morning with the following symptoms and signs: Headache, pain over the kidneys, constipation, slight pain in right iliac fossa, slight, dry cough; heart, lungs, liver and spleen normal. There is an eruption of flat, rose-colored, irregular macules scattered over the chest, abdomen and legs, and about the anus. General glandular enlargement is present, the right femoral glands being also painful and tender. (See Chart A.)

January 30: No malarial parasites in blood; leucocyte count 5,400; urine normal.

January 31: Glands in right femoral region more enlarged, tender and painful. There is headache and slight abdominal pain.

February 2: Muttering delirium, nervous twitching and subsultus are present this morning. The skin is mottled and the eruption increased on chest, abdomen, neck, face, legs and about the anus. Tongue coated and dry, pulse dicrotic. Femoral glands smaller.

February 3: Breathing is thoracic and shallow, face flushed; femoral glands painful; eruption more dusky. The pulse is rapid and irregular.

February 4: No change. Blood shows no malarial parasites; leucocyte count, 4,300.

February 6: The patient feels better this morning; the pulse is of good tension, the eruption fading.

February 9: Improved. Patient looks brighter and feels very well. His mental condition is peculiar, not normal.

February 10: Delirious all night and to-day. Face flushed; pulse remains fairly strong.

February 11: Improved, quiet no pain.

February 13: Improved, hungry. The pulse is good and the rash disappearing. Urine normal.

February 16: The patient has improved. He has no pain, the pulse is strong, the eruption and glandular enlargement have disappeared.

February 19: The Widal reaction is negative after one hour.

CASE B.—*H. D. P.; age, 34; teamster.*

Family history.—Negative.

Personal history.—The patient has had diseases of childhood, "typhoid-malaria" in 1894, dysentery in 1903. There is no history of syphilis or gonorrhœa.

Present illness.—February 2, 1906: The patient has felt badly for five days and has had headache, pain in the back and limbs and in abdomen, and the appetite has been poor. There was no chill and but slight cough. Two days ago he noticed enlarged glands in the right axilla and right groin. Yesterday he had diarrhœa. He was admitted to the hospital to-day suffering from fever, pain in the head, back, legs, anus and abdomen, enlarged and painful lymphatic glands in the right axilla and groin, and diarrhœa.

Physical examination.—The heart is normal; dry râles are heard over the upper lobes of both lungs. The abdomen is tender around the umbilicus, the spleen enlarged. A rose-colored, irregular, macular rash shows on the head, trunk and limbs. There is a general enlargement of the superficial lymphatic glands, more marked in the right axilla and groin. The tongue is moist and has a white, central coat and red edges. No malarial parasites found in the blood. (See Chart B.)

February 3: No malarial parasites. The patient is dull, the face flushed, the axillary and inguinal glands painful.

February 4: There is no change. Leucocyte count, 3,200; no malarial parasites.

February 5: The patient appears better this morning. The pulse is of good tension, the eruption fading. There was a marked chill after a plunge bath.

February 6: The eruption is fading, the pulse is good, the tongue dark and dry. No malarial parasites in the blood. A differential count of white cells shows: Small lymphocytes 20, large lymphocytes 8, polymorphonuclears 60, eosinophiles 2, transitionals and large mononuclears 4, per centum.

February 9: Still improving. A gland was removed from the right groin for examination.

February 10: Improving. Face flushed, eyes injected, mouth dry, and the tongue shows a yellowish coat. The pulse is of good tension, the eruption confluent and fading. No malarial parasites in the blood.

February 12: Patient is still improving. He sleeps well. Bacteriological examination of the excised gland was negative.

February 13: The patient is hungry, the eruption has disappeared, the glandular enlargement is less marked and the urine is normal.

February 19: Patient is still improving. Widal reaction was negative after one hour. No malarial parasites found in the blood.

Lieutenant Bruns made daily notes on these cases, but when there was no change in the condition or no new examination mentioned, the remarks have been omitted. Both patients received cold baths during the progress of the disease and the charts are probably modified by them. While the notes do not indicate it, such is probably the explanation of the two marked drops of temperature shown by Charts B. A satisfactory diagnosis was never made on either case, although both were reported as being typhoid fever.

We do not maintain that these cases were *tsutsugamushi* disease, but they certainly present enough points of resemblance to it to make it worth while for medical men in the Philippines to keep the matter in mind, should they have the opportunity of investigating similar infections.

ACKNOWLEDGMENT.

We desire to express our thanks to those assisting us in this study, and particularly to Professor Miyajima and his fellow-workers from the Imperial Institute for Researches of Infectious Diseases, to whom we are indebted for the opportunity to see what we did of *tsutsugamushi* disease and for such knowledge as we have of the articles published on it in Japanese, as well as for the information they gave us concerning their own work. We are also indebted to Lieutenant Bruns, for his notes on the Camp Connell cases.

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Chart 1.

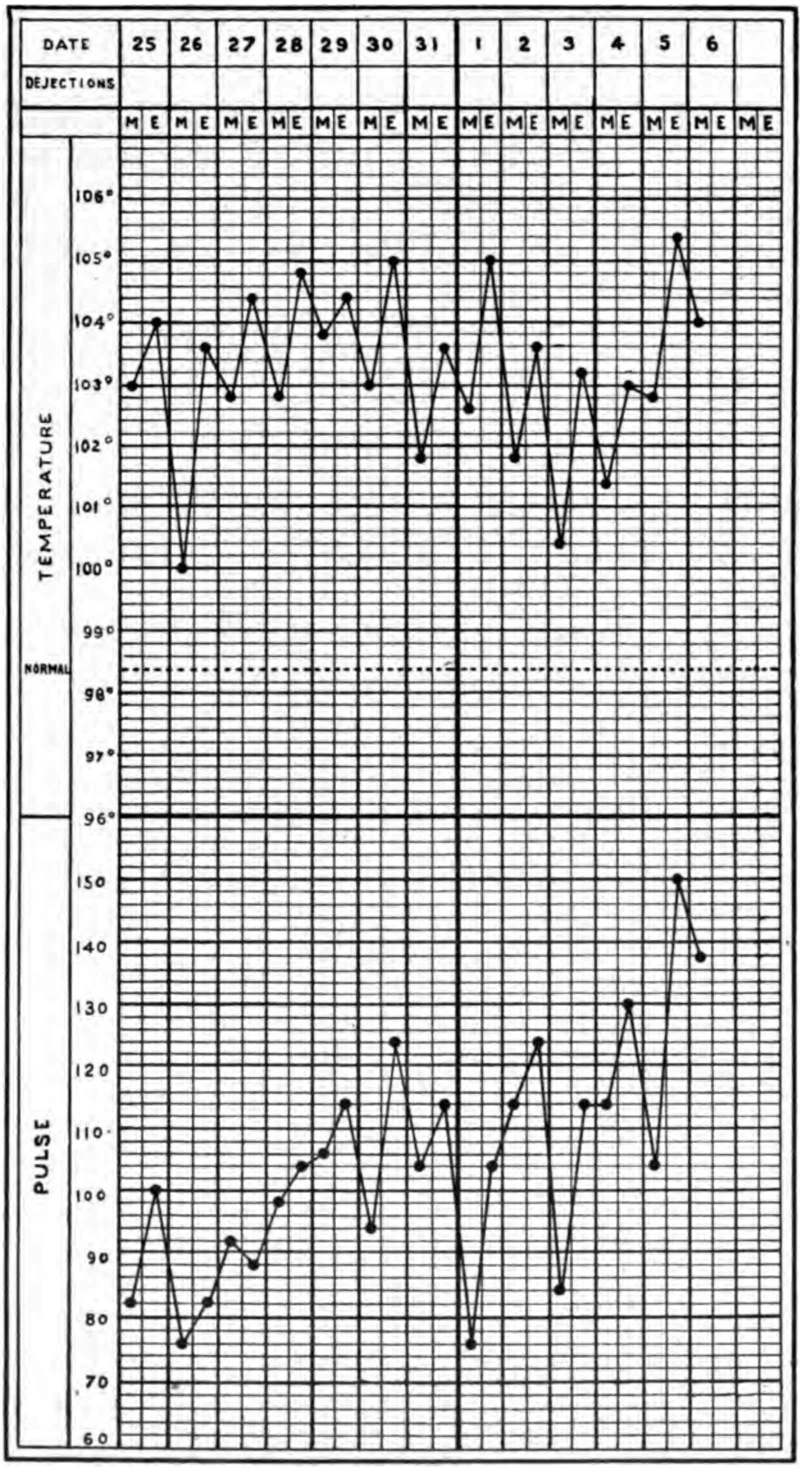
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Chart 2.

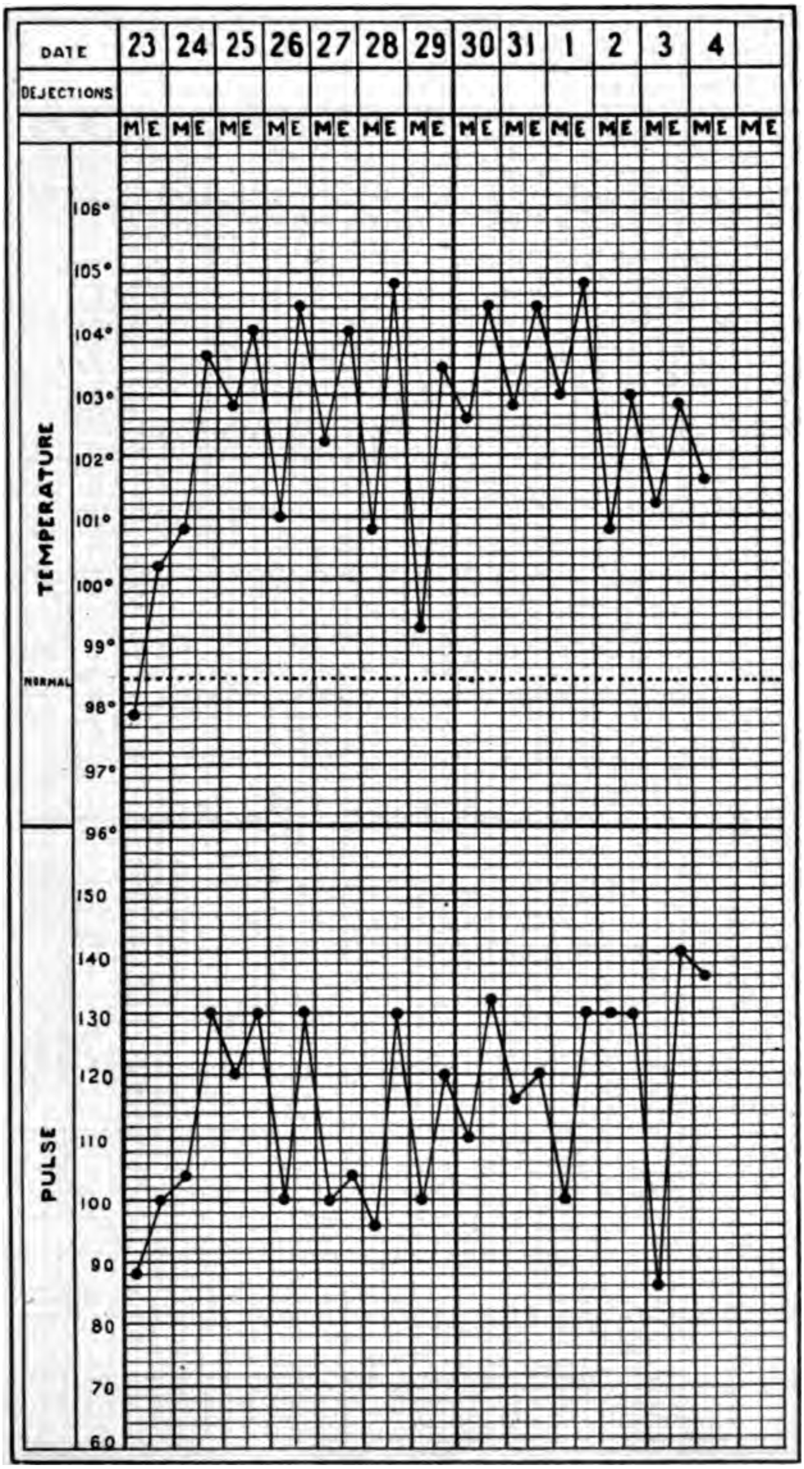
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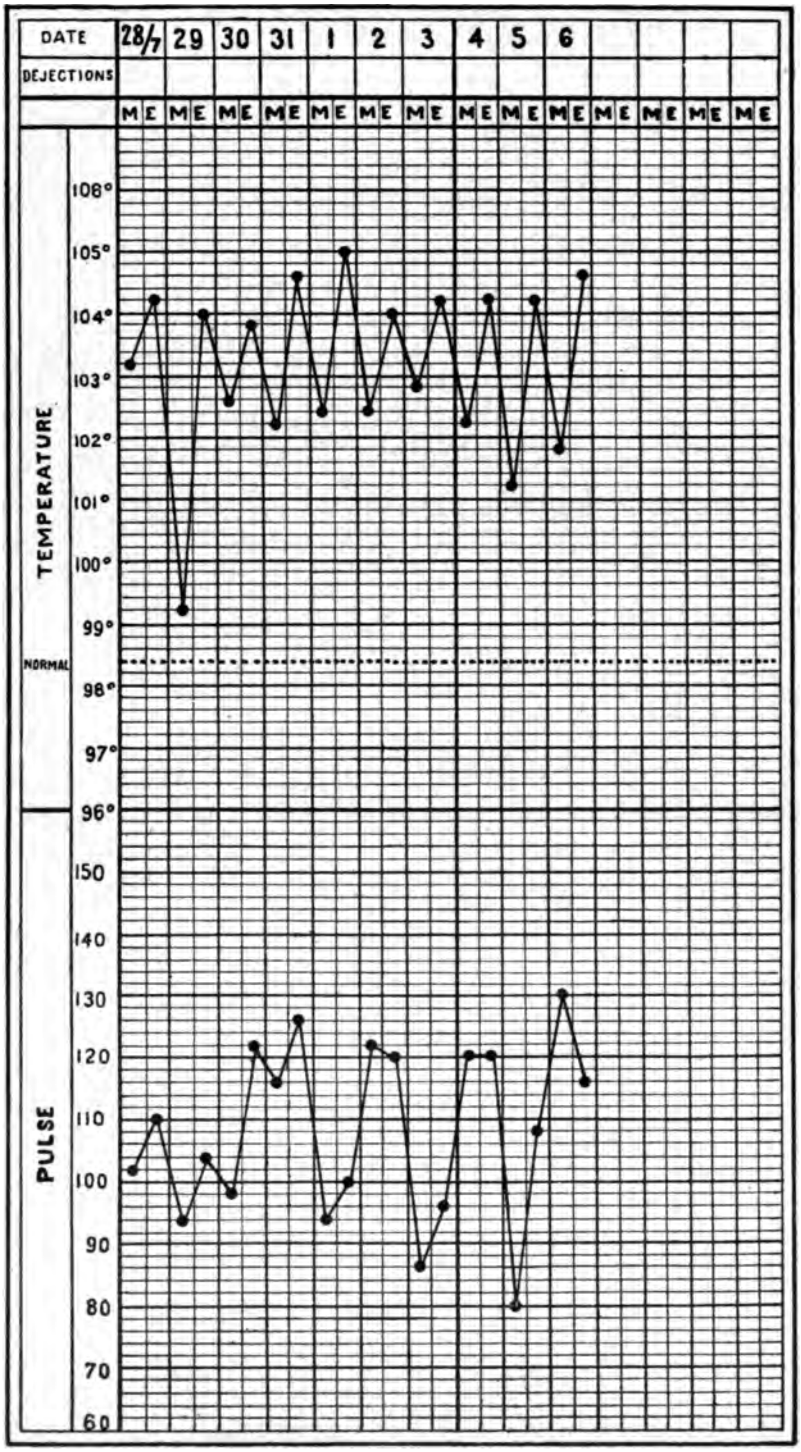
Chart 3.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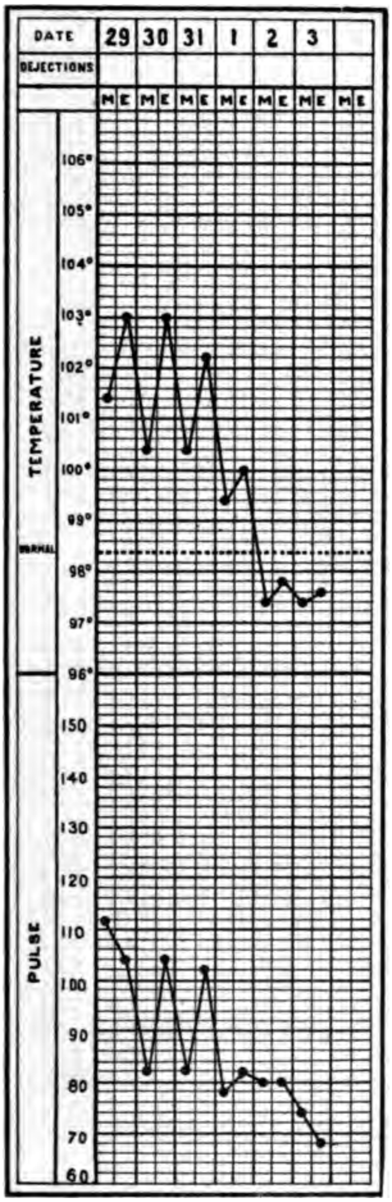

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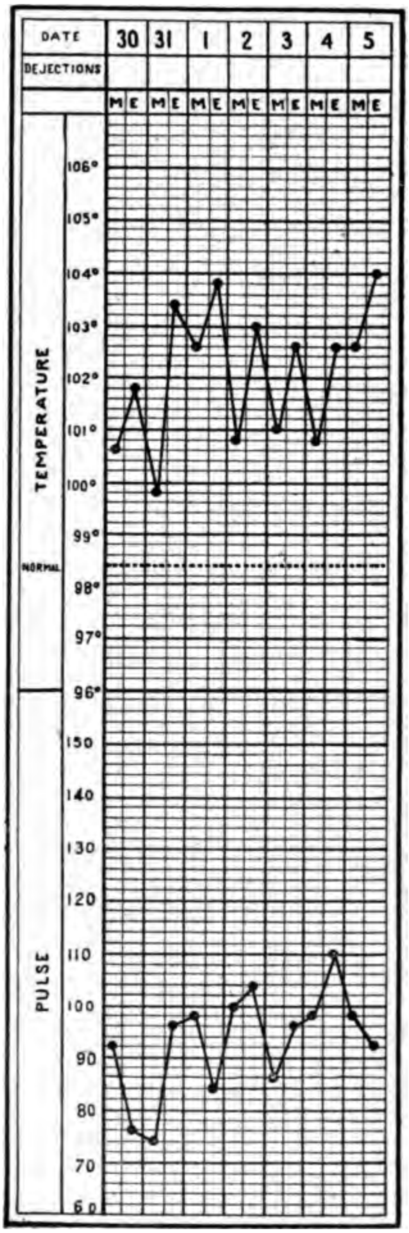

Chart A.

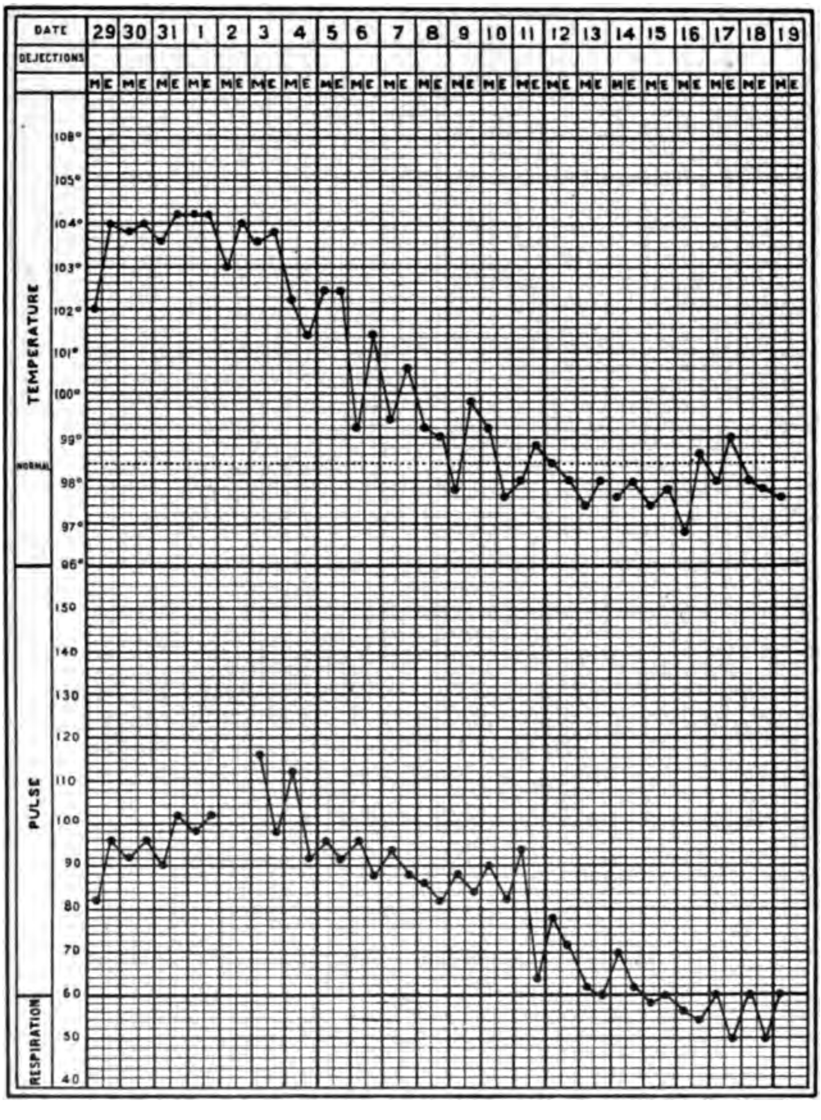
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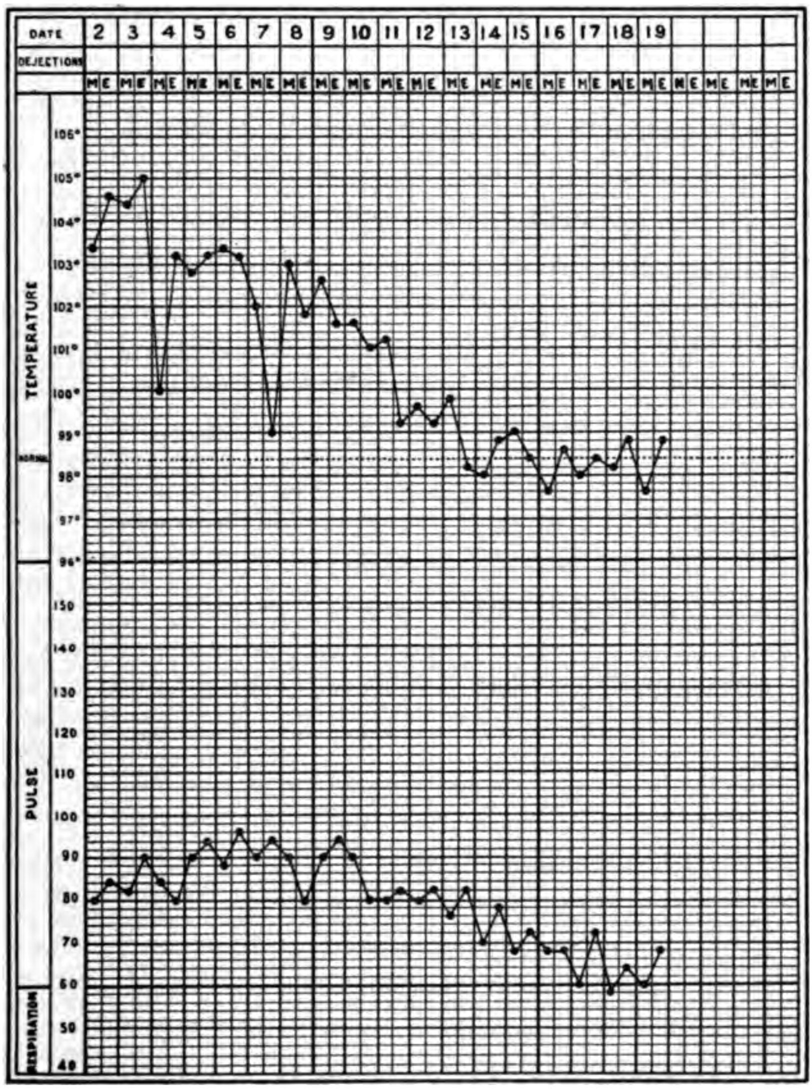
Chart B.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A SERIES OF CASES OF TROPICAL INFANTILE DYSENTERY WITH A HITHERTO UNDESCRIBED BACILLUS AS THE CAUSATIVE FACTOR.

[Preliminary report.]

By FRED B. BOWMAN.
(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

During the latter part of July and the month of August, 1907, quite a severe epidemic of infantile dysentery prevailed in and around Manila, and the following observations were made upon a series of cases from the private practice of Dr. Musgrave. It was evident, judging from the suddenness of onset, the severity of the attack and the extremely long period of convalescence in some instances, that we were dealing with a severe infection caused by some pathogenic intestinal organism, probably the Shiga bacillus itself or one of the many varieties of *B. dysenteriæ.* It was consequently deemed of importance accurately to study this epidemic and therefore I secured as much material as possible.

In all cases fæcal matter was obtained either in a sterile dish or on a square of sterile gauze, and the specimen were transferred to the laboratory as quickly as possible for examination. A brief history of each case follows, with an outline of the technical procedure adopted in isolating the organism.

CASE I.—*Infant S.*

Severe, acute dysentery with recovery.—A strong, well-developed infant, weighing 8½ pounds at birth and 19 pounds at 9 months of age. It was breast fed during the first four months and mixed feeding was resorted to until the end of the seventh month. For two months before the attack of dysentery the child was fed entirely on artificial food which consisted of a percentage modification of milk and cream with a small amount of fruit juice once daily. The infant's growth and development were entirely satisfactory before and after the attack. The dysentery developed rather suddenly during the night, the symptoms being cramps, fever and frequent stools. The latter at first were watery and contained mucus, but within six hours they showed small quantities of blood. For the next few days the dysentery was quite severe; it was characterized by pain, tenesmus and fever ranging from 38° to 40° C. During this time the stools were between ten and twenty-five in number during twenty-four hours, consisting almost entirely of blood and mucus. The symptoms gradually subsided and convalescence was well established on the fifteenth day. The treatment consisted of enemas of 1–2,000 solution of an organic acid peroxide and a very restricted diet, with paregoric in sufficient quantity to control the pain.

Cultures were made from the fresh specimen passed on the morning of the third day of the disease. This was sent to the laboratory contained in a small square of sterile gauze.

CASE II.—*Infant L.*

Moderately severe, acute dysentery with recovery.—The patient was an unusually well-developed, strong, healthy boy 2 years old, weighing 9 pounds at birth and 28 pounds at 1 year of age. Diarrhœa developed, following a period of malaise lasting about twenty-four hours, with about one degree of fever. The character of the bowel discharges rapidly changed to the typical bloody mucus stools of acute dysentery and continued in this manner for about ten days with from six to fifteen passages a day. Convalescence was slow, and complete recovery did not take place until the end of about one and one-half months. At first the prostration was considerable, temperature 38° to 39°.5 C. with a moderate amount of tenesmus and loss of appetite.

The treatment consisted of the same bowel irrigations as in Case I together with occasional doses of castor oil. Pain was controlled by the use of paragoric.

Cultures were made from a fresh specimen of the stool obtained on the second day of the disease.

CASE III.—*Infant B.*

Mild, acute dysentery, with subsequent recurrence and recovery.—A healthy infant 10 months old, breast fed from birth and weighing 22 pounds at the time he was taken sick. Acute diarrhœa suddenly developed during the night and within the next twenty-four hours the stools changed in character to those characteristic of dysentery and so continued for eight or ten days, with from three to ten bowel movements a day. Convalescence was quickly established, but a recurrence similar to the first attack took place at the end of two weeks. Convalescence was again rapid and the child has since remained perfectly well. There was no fever at any time, the tenesmus was not very great and the quantity of blood passed was inconsiderable. There was no loss of appetite and but little toxæmia. After the first two days, the bowel movements could be fairly well controlled by simple irrigation of the colon.

Cultures made on the first day of the disease. No pathogenic organism was found and the bacillus to be described below as present in the two preceding cases could not be isolated.[1]

CASE IV.—*Infant T.*

Severe, acute diarrhœa with recovery.—This infant was 5 months old, weighing 9 pounds at birth. It continued to thrive on breast milk during the first two months. At this time it became necessary to change to artificial food because of failure of the breast supply. From that time until the development of the diarrhœa, assimilation of food had not been satisfactory. Percentage feeding with a large range of variation in both the proteid and fat content was tried without success. Vomiting was frequent and emaciation became quite marked, so that at the time of the development of the diarrhœa the child was already in a very much exhausted condition. The diarrhœa lasted for about two weeks, with from three to fifteen passages a day, and in a few instances small streaks of blood and a considerable amount of mucus were found in the stools.

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[1] Since these observations were made Case III, three months after recovery, developed an acute dysentery similar to the first attack. Bacillus "S" was isolated, being agglutinated by the specific rabbit serum in high dilutions (1–20,000).

Cultures were made on the fourth day of the disease.

The technique used in the first two cases was also employed in this one; it will therefore be unnecessary to give a separate description in each case.

THE ORGANISM.

Smears made from a portion of the mucus of the stool showed two types of bacilli; one a rather large organism with rounded ends, and the other in comparison, extremely small. A series of four alkaline bouillon tubes was inoculated with the material from the mucus portion of the specimen and the tubes were allowed to stand four hours, when a very slight cloud could be observed near the surfaces of the medium. A series of four alkaline agar tubes at 45° C. was made from each tube, plated and placed in the incubator for twenty-four hours at 37° C., when I marked the colonies present; at the end of another twenty-four hours several new colonies had appeared. There were very small and of an intense blue color, the original colonies 24 hours old being creamy-gray. Transfers to alkaline agar were made from each type of colony and placed in the incubator for twenty-four hours, after which time subcultures were made. The results are tabulated below. (See Table I.) I have termed the 24-hour growth "C" and the 48-hour one "S". Stained specimens of bacilli from each tube agreed in morphology with those found in the smears made from the fresh mucus.

Later, after obtaining the reaction of the organism in lactose bouillon, I used another method for its isolation. Fermentation tubes were inoculated directly from the plate colonies, and after the reaction had identified the organism, it was transferred from this medium to agar, subcultures being made from the latter.

A study of Table I shows the following characteristics which distinguish *Bacillus "S"* from *Bacillus coli*. *Bacillus "S"* seems to be somewhat smaller and more delicate than *B. coli*. Its motility is quite marked and is of a wriggling and twisting character. Coagulation is delayed in milk and the litmus present is completely reduced. It forms no gas in lactose-litmus and there is profuse growth. The indol reaction is negative.

Fermentative tests were also made using the colon bacillus isolated from the specimen taken from Case I as a control.

TABLE I.—*Showing cultural characteristics of Bacillus "S" as compared with B. coli isolated from the same stool.*

Bacillus.	Agar-agar.		Glucose-agar.	Lactose-agar.	Gelatin.	Old serum.	Potato.	Lactose-litmus.	Mannite-litmus-agar.	Litmus-milk.	Morphology motility.	Indol reaction.
	—1 per cent.	+1 per cent.										
Bacillus coli:												
24 hours	Typical colon.	Typical colon.	Much gas, growth.	*Much* gas.	No liquefaction.	Typical colon.	Profuse yellow-brown growth.	Much gas and growth.	Gas, acidified.	Acidified, coagulated, fæcal odor.	Size, 0.7×1.3 μ practically nonmotile. Gram—negative. Stains with all stains.	Positive.
48 hours	do	do	do	do	do	do	do	do	do	do		Do.
72 hours	do	do	do	do	do	do	do	do	do	do		Do.
Bacillus "S:"												
24 hours	do	do	do	*No* gas.	do	do	Almost imperceptible, pure, white growth.	Growth. No gas.	*Much* gas, acidified.	Peptonized, reduction of litmus, no fæcal odor.	Size, 0.5×.075 μ small and thin. Extremely motile. Stains with all the aniline stains.	Negative.
48 hours	do	do	do	do	do	do	do	do	do	do		Do.
72 hours	do	do	do	do	do	do	Heavier growth	Slightly decomposed with gas formation.	Completely decomposed with gas formation and decolorized.	Slight coagulum.		Do.

TABLE II.—*Bacillus* "*S*."

Media.	24 hours.	48 hours.	72 hours.
Lactose	—	-	—
Maltose	+	+	+
Saccharose	+	+	+
Glucose	+	+	+

The fermentation tubes inoculated with *B. coli* showed more gas in the lactose medium than in any of the others.

PATHOGENICITY.

Transfers were made to slant alkaline-agar tubes and placed in the incubator at 37° C. for twenty-four hours. The slants were completely covered with the growth and each was then in each instance suspended in 20 cubic centimeters of normal salt solution. One cubic centimeter of this suspension (0.05 of an agar slant) injected intraperitoneally, killed a guinea pig in twelve hours, 0.04 of a slant was fatal in less than twenty-four hours. Rabbits were much less susceptible, 0.1 to 0.07 of a 24-hour slant, inoculated intraperitoneally, killing a rabbit in from twenty-four to thirty-two hours. Similar conditions were found in both rabbits and guinea pigs at autopsy, there was injection of the tissues about the point of inoculation, enlargement of lymphatic glands, a large amount of sero-purulent exudate, and both the liver and spleen were congested; stained smears from the exudate and from the liver and spleen showed the presence in pure culture of a small bacillus, identical morphologically with the original organism. Hanging drops of the exudate demonstrated an organism having a marked motility and in some of the specimens examined, an almost cholera-like character. Subcultures made from the exudate developed in a manner identical with that of the original organism. A rabbit inoculated subcutaneously with peritoneal fluid from a guinea pig dead of the infection developed a large, fluctuating abscess and at the same time showed a very marked diarrhœa.

Suspensions of the bacillus in salt solution were fed to a monkey through a stomach tube for four succesive days, after the gastric acidity had been neutralized with sodium carbonate. The monkey became ill, at the end of two weeks the animal was killed and autopsy performed. There appeared to be a certain amount of inflammation of the large intestine and cæcum and of a portion of the small intestine adjoining. Sections were made and examined microscopically, but they showed nothing which would account for the reserve prostration. Cultures from the intestine were negative. However, the organism was recovered from a stool passed three days after feeding the bacterial suspension.

After the organism had been grown for one month its pathogenicity was again tested. Comparatively large doses failed to kill either guinea pigs or rabbits. It is evident from this that Bacillus "S" rapidly loses its pathogenicity. The original fatal dose was again obtained after passage through guinea pigs.

TOXICITY.

The filtrate from living cultures.—Two flasks, each containing 150 cubic centimeters of sterile bouillon, one being 1.5 per cent alkaline, the other two per cent acid, were inoculated and allowed to grow at 37° C. for twenty-four hours. The cultures were then each passed through a Berkefeld filter, and the filtrate injected in large and small amounts intraperitoneally into guinea pigs, and intravenously into rabbits. The result was negative. The cultures after growing for seven days in alkaline and acid bouillon respectively were filtered and the filtrate inoculated into rabbits and guinea pigs with negative results.

A search was then made for an endotoxin. Six complete slants of agar in tubes were inoculated and the organism allowed to grow twenty-four hours, it was then suspended in salt solution and placed in a shaking machine for eighteen hours. The filtrate was injected into guinea pigs and rabbits, without result.

Suspension of killed cultures.—Suspension of 24-hour growths of the bacilli were placed in an incubator at 60° C. for one hour, and plates were then made demonstrating the sterility of the suspension. Two guinea pigs were inoculated each with 2 cubic centimeters of the suspension; one rabbit received 2 cubic centimeters intravenously. After twenty-four hours the guinea pigs were both dead, the rabbit still alive. At autopsy it was demonstrated that the peritioneal cavity of each guinea pig contained a large amount of sero-purulent fluid. However, smears and cultures from this were negative. At the end of forty-eight hours the plates made from the killed suspension were examined. They were sterile.

Agglutination tests.—As all four cases occurred in private practice it was not possible to obtain blood from each patient. Blood in very small amount was obtained from Case I on a slide, and although accurate quantitative tests could not be made, those which were conducted were very suggestive.

The blood from Case I was diluted with salt solution 1 to 50 and hanging drop preparations made with controls in each case. Table III shows the result.

TABLE III.—*Serum from Case I.*

Organism.	Agglutination.
Case I, *Bacillus* "*S*"	+
Case II, *Bacillus* "*S*"	+
Case III, *Bacillus* "*S*"	+
Bacillus typhosus	—
Bacillus dysenteriæ	—
Bacillus coli	—

One rabbit (number 3227) was rendered immune to the original *Bacillus "S"* and another (number 3229) to *Bacillus "S"* isolated from Case II. Living cultures were used and inoculated intravenously in increasing doses. Tests were made constantly and the agglutinative limit was reached in six weeks, each rabbit was then bled and agglutination reactions made as shown in Tables IV and V.

TABLE IV.—*Serum from rabbit immunized to Bacillus "S" (Case I) incubated at 37° C. for three hours.*

Bacillus.	1-50.	1-100.	1-200.	1-400.	1-800.	1-1,600.	1-3,200.	1-6,400.	1-12,800.	1-25,600.
"*S*"	+	+ +	+ +	+	+ + +	+ + +	+	+	+?	—
"*L*"	+	+	+ +	+ +	—	+ + +	+ + +	+	+	—
"*T*"	+?	+	+	+ +	+	+ +	+	+	+?	·
Coli	—	—	—	—	—	—	—	—	—	—
Dysenteriæ	—	—	—	—	—	—	—	—	—	—
Typhi	—	—	—	—	—	—	—	—	—	—

TABLE V.—*Serum of rabbit immunized to Bacillus "S" (Case II) incubated at 37° C. for three hours.*

Bacillus.	1-50.	1-100.	1-200.	1-400.	1-800.	1-1,600.	1-3,200.	1-6,400.	1-12,800.	1-25,600.
"*L*"	+ +	+ +	+ + +	+ + +	+ +	+ +	+	+	+	+
"*S*"	+	+	+ +	+ +	+ +	+	+	+	+	+?
"*T*"	+	+	+	+ +	+	+	+	+	+	—
Coli	—	—	—	—	—	—	—	—	—	--------
Dysenteriæ	—	—	—	—	—	—	—	—	—	--------
Typhi	—	—	—	—	—	—	—	—	—	--------

All the tests were made macroscopically, test tubes containing suspensions of the organism in normal salt solution being used. After each dilution was made, all were placed in the incubator at 37° C. for three hours before being examined. Controls were made in each case. The seemingly absolute specificity of the serum from each rabbit for the three organisms isolated is very striking, Shiga, colon, and typhoid bacilli being unaffected in either case. Examination at the end of eighteen hours revealed absolutely no change in the homogeneity of the suspensions of the latter organism.

Summary.—During the past summer, especially during the months of July and August, several severe cases of infantile dysentery developed in Manila. A bacillus was isolated which culturally and morphologically resembled in some ways *B. dysenteriæ,* in others *B. coli* and *B. typhosus.* The specific agglutinins developed in animals through inoculation of this bacillus did not react with *B. dysenteriæ. B. coli* and *B. typhosus,* but organisms isolated from three other cases of dysentery were agglutinated in high dilutions, each by the specific serum of the other.

Serum from one patient agglutinated the bacillus isolated from the same patient, yet did not agglutinate other organisms from the same source.

Conclusions.—Intestinal organisms, especially the Shiga bacillus, exhibit such varied cultural and agglutinative characters when growing under different conditions and in different localities, that it is very difficult to classify them. From the above observations and a search through the literature we are led to believe that the bacillus isolated from these cases has hitherto not been described as one of the exciting factors in dysentery, but the specific character of the serum of one these cases and of that from rabbits immunized against *Bacillus "S"* seems to show conclusively that this bacillus was the cause of the epidemic of infantile dysentery which has been described.

PLAGUE PROCEDURE IN HONGKONG.

By Dr. J. M. Atkinson.[1]
(Principal Civil Medical Officer Hongkong.)

The plague procedure now in force in the colony of Victoria is as follows: 1. Notification. 2. Isolation. 3. Disinfection. 4. Segregation of contacts. 5. Cleansing operations.

1. *Notification.*—The main difficulty has been that the Chinese will not notify the authorities of the occurrence of the disease, preferring to hide their cases, and to deposit the body in the street after death. This procedure applies also to persons dying from other infectious diseases, such as smallpox, diphtheria, etc., and it is to a great extent caused by the dread these people have of disinfecting operations. This is proved by the fact that the percentage of bodies so deposited increased very considerably after the enforcement, in 1903, of the disinfection of houses on either side of the ones in which plague-infected rats had been found, in accordance with the recommendations made by Professor Simpson. The percentage of bodies so found was 32.7 in 1903 as compared with 25.1 in 1898.

2. *Isolation.*—Victims attacked by the disease are treated in the infectious disease hospitals at Kennedy Turn, one of which is a Government institution conducted as such institutions are in the Occident, the other, a native branch of Tung Wah Hospital, administrated by the Chinese, but under our sanitary supervision.

District plague hospitals have been established in Victoria and Hongkong during the past two years in order to obviate the necessity of removing the patients to such a distance as the situation of the Kennedy Turn hospitals; they are also allowed to be treated by their own doctors, the intention being, by these concessions, to obtain the coöperation of the Chinese and to prevent or minimize the depositing of plague bodies in the streets.

3. *Disinfection.*—This is rigidly enforced, compensation being given for any damage done to clothing. The process of disinfection consists

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[1] Read at the Fourth Annual Meeting of the Philippine Islands Medical Association, March 3, 1907.

in the removal of all bedding, clothing, curtains, mats, etc., to the disinfecting station, these articles being tied up into bundles with large sheets of calico and then put into baskets which are carried by coolies, government clothing being supplied temporarily to replace the personal garments of the occupants of the infected houses. The walls and floors of the house are then sprayed with a 1–1,000 solution of corrosive sublimate, the floors are scrubbed with a 5 per cent solution of Jeyes's fluid, the drains are flushed, all rat runs are opened and crude carbolic acid poured into them, afterwards they are filled with broken glass and stopped with cement.

4. *Segregation of contacts.*—At the beginning of an outbreak the infected premises are evacuated and the residents kept under medical supervision for twelve days in blocks of houses rented for the purpose of accommodating them, they being allowed to carry on their usual vocations during this period.

5. *Cleansing operations.*—In the spring of 1903, the governor, Sir H. A. Blake, S. C. M. G., decided if possible to obtain the coöperation of the Chinese in the work of sanitation. He took over a district in the most plague-stricken portion of the city and endeavored to show what could be done by a thorough cleansing of houses and clothing by the people themselves. The work was begun in the winter of 1903–4 and as a practical result we have been able to obtain the coöperation of the Chinese in the "cleansing operations" and now every winter a general cleansing of the houses is effected by these people. Hot water in portable boilers, soft soap and Jeyes's fluid are supplied, the sanitary department removing all the rubbish and refuse from the houses. The procedure is as follows: Each householder receives a notice in writing stating that in two days' time a visit of inspection will be paid by the sanitary inspector and if the premises are found to be dirty, they will be cleaned by the sanitary authorities. These notices are sent seriatim to the different houses, beginning with each health district simultaneously. In very few instances has it been found necessary to enforce government cleaning.

Cleanliness is undoubtedly the bed rock of sanitation, and to insure it both of persons and houses, the coöperation of the people must be secured, this aid being more especially necessary when we deal with an alien race, such as the Chinese.

It is an almost hopeless task to expect to stamp out plague entirely in Hongkong, because we are, owing to our geographical position, constantly exposed to reinfection from the neighboring countries, the disease being practically endemic in Canton, Swatow and Amoy. Many insanitary areas and buildings have been allowed to be erected, and it is only by their reërection on improved plans and by the rigid prevention of overcrowding that plague, or any other infectious disease can be eliminated from Hongkong. This rebuilding will of necessity be a slow process, but it is being steadily effected by means of the new public health and building ordinance and by the government each year resuming some of the most insanitary areas of the town.

PLAGUE PROCEDURE, 1904.

The following rules have been adopted and carried out:

1. On finding a suspicious case of plague, notify the medical officer of health at once.

2. Removals of sick must be to the district hospitals when they are established, or to the existing hospitals, as may be decided by the medical officer.

3. When a guard is required, the police must be applied to, the district watchmen's committee being unable to arrange for the employment of district watchmen. Further, when anyone reports a case of sickness or a death in a house voluntarily, the guard, pending the diagnosis of the case, may be dispensed with, provided that the occupants of the infected floor are willing to give their clothes up for disinfection at once. In such a case the tenants of the infected floor will be free to go where they like after giving up their clothing, and if the case should be returned as one of plague, the disinfection of the floor can then be proceeded with.

4. On receiving confirmation of the suspicion of plague in a house, proceed without delay to the house with the necessary assistance and equipment, and disinfect.

5. The disinfecting operations are to be confined to the floor in which the case occurred, unless there is reason to believe that the sick person frequented other floors.

6. The whole of the house should, however, be cleansed and the tenants of the noninfected floors may do this themselves if they are willing. Disinfecting fluid (Jeyes's) to be given for that purpose.

7. In cases where it is considered necessary to pull down ceilings, etc., in other than infected floors, the tenants may, if they wish, assist by first removing their furniture and afterwards clearing away the débris; but the board's officers must see that the débris is properly sprayed before removal, so as to lay the dust, and that the débris is put into the dust carts and not made use of by the people. The joints, etc., bared by such removal of ceiling or linings should also be sprayed.

8. The cleansing and disinfection of the infected floor must be wholly done by the board's officers.

9. People turned out of houses on account of plague must always be offered shelter in the block of houses rented by the board for this purpose, and help in the removal of their effects to such shelters must be offered.

10. The disinfecting operations are to be done in the manner and order laid down in the attached directions:

DISINFECTION OF INFECTED PREMISES.

This is carried out by a European officer assisted by eight colored foremen, a Chinese foreman, and a varying number of coolies. As soon as it is known that a case of the disease has occurred at any house, a Chinese constable is sent from the nearest police station to detain all persons found therein (By-law 22, Ordinance 15 of 1894), and the officer in charge of the disinfection proceeds to the house to ascertain how many persons are detained there. He then procures, either from the matshed at Praya East or from the disinfecting station, as many suits of government clothing as are needed for the persons so detained, and having thus provided these persons with clothing, he removes their own clothing, bedding, curtains and carpets to the steam disinfecting station, the clothing being tied up in sheets dipped in a solution of Jeyes's fluid and conveyed through the streets in baskets; persons who are able to obtain new or clean clothing from some uninfected premises are, however, not detained after they have discarded their infected clothing and have handed it to the inspector for disinfection. New goods, silk clothing which has not been recently worn, furs and leather goods are not removed to the steam disinfector, but must as a general rule remain on the premises until they have been fumigated. When the clothing, etc., is returned (in the course of some two hours) from the disinfecting station, the persons who have been detained are required to put on their own clothing and must then leave the premises for some five or six hours while the dwelling is disinfected and cleansed. The government clothing is returned to the disinfecting station to be steamed before it is again used. The people so displaced from their homes are at liberty to make use of the board's matshed shelters until the processes of disinfection of the premises are complete.

The disinfection of the premises consists in the spraying of the walls with a solution of bichloride of mercury (1 in 1,000) or fumigation with free chlorine obtained by the addition of diluted sulphuric acid to chlorinated lime (1 quart of a 1 to 8 solution of the acid to each pound of the chlorinated lime). Floors and furniture are scrubbed with a solution of Jeyes's fluid and the walls are then lime-washed, chlorinated lime being added to the lime wash in the proportion of one-half pound to the gallon.

PLAGUE MEASURES, 1906–7.

There are at present four plague inspectors for the city of Victoria, and one for Kowloon. There are eleven colored foreman interpreters, one for each district of the city of Victoria and one for Kowloon, who supervise the work of the rat catchers, assist in the house-to-house cleaning, and act as interpreters to the inspectors where necessary. There are five gangs in the city of Victoria each consisting of one Chinese foreman, one artisan and seven coolies. Two inspectors have each one and one-half gangs, and the other two have a gang each, while Kowloon also has a gang consisting of a Chinese foreman, two artisans and ten coolies.

During nonepidemic periods the whole of this staff is engaged in house-to-house cleaning work, about ten houses or thirty floors a day being dealt with. Each tenant receives three days' notice, in writing, requiring him throughly to cleanse his premises. On the day fixed, the gang attends in the street opposite the houses named and supplies hot water and soap solution to the tenants, it cleans out all empty floors, basements, etc., the tenants themselves cleansing their own premises without assistance from us. The refuse turned out during this operation is removed by the gang to the nearest dust boat. The soap solution is also used by the tenants for washing their bed-boards, etc., in the street or on the veranda.

When the cleansing work is completed by the tenants, the inspector visits every floor, accompanied by the foreman interpreter and some of the coolies with a bucket of disinfectant (liquid fuel) and some mops; this liquid is applied to the sides and corners of the floors, to the skirtings, around the partitions of the cubicles, and to the stairs, under the personal supervision of the inspector. At this visit, when the floors are clear of furniture, and other incumbrances, the inspector makes special note of the condition of the ground surfaces, the absence of gratings to drain-inlets and ventilators, and the presence of rat runs, and all these matters are dealt with by legal notice at once. The tenants are requested by notice, to permit their bedding and spare clothing to be steamed, in order to destroy fleas and other vermin and their ova, but heretofore in Victoria they have persistently refused to allow this to be done, even though compensation is offered for all articles damaged. Should a case of plague appear in a house, the floor on which the case occurs is disinfected by the plague staff, the walls being sprayed with corrosive sublimate, and the floor and bed boards washed with Jeyes's fluid (half a pint to the gallon); crude carbolic acid is poured into the rat runs, which are then filled up with cement; and the clothing and bedding is sent to the disinfecting station to be steamed. The remaining floors of the infected house are cleansed by the tenants in the same manner as in the house-to-house cleaning. Should there be any ceilings or stair linings in the infected house, these are removed and compensation is paid for them, if the case has been duly reported, while illegalities are dealt with by notice. The compensation in the case of Chinese is assessed separately by the kaifong of the districts and by the plague inspector, and the assessments are dealt with by a committee of the sanitary board. The kaifong are appointed by the Tung Wah hospital for the city of Victoria, and in Kowloon by the inhabitants of Kowloon Point, Yaumati, and Hunghom, respectively.

Any spare time at the disposal of the plague inspectors is occupied in paying special visits to houses in which cases of plague have occurred in the previous season, so as to be sure that they are free of rat runs and provided with impervious ground surfaces.

The Chinese have established public dispensaries and also district plague hospitals, which in the city of Victoria are managed by a committee of which the registrar-general and the two Chinese members of the sanitary board are members; in Kowloon, a purely local committee manages the dispensary and the hospital. These institutions are supported by voluntary contributions, and each is in charge of a licenciate of the Hongkong College of Medicine for Chinese, who sees outpatients at the dispensary, performs vaccinations, visits patients in their own homes, and treats those in the district hospital. Notice of cases of infectious diseases are given by these doctors to the nearest district office, and in the case of plague, the patient may be treated in the district hospital.

FLEAS ENCOUNTERED IN HONGKONG.

In October last, seeing the importance attributed by the Indian Plague Commission to the agency of fleas in carrying the pest infection, I instructed Mr. Gilson, the colonial veterinary surgeon, and Dr. Heanley, the assistant bacteriologist, to report to me concerning the species of fleas and rats met with in Hongkong.

The varieties of fleas are as follows:

(a) *Ctenocephalus canis* Curtis.[2] This flea is found on cats and dogs, but it is frequently taken on man also. It is a small flea, variable in size and of a dark color. It is not so nocturnal in habits as the other fleas. Dr. Heanley and Mr. Gilson found it on *Mus decumanus* and on dogs and men.

(b) *Pulex cheopis* Rothschild or *pallidus* Tasch. This is the common rat flea and is met with on *Mus decumanus, Mus rattus* and the muskrat. It is small, light-colored and more or less nocturnal in its habits. In Hongkong it is found more frequently on *Mus decumanus.*

Normally, the rat flea (*P. cheopis* Rothsch.) is rarely found on man The insects will, however, attack guinea pigs and accordingly it would be advisible to set free some guinea pigs in a room where a case of plague has occurred. The infection of guinea pigs by *Pulex cheopis* Rothsch. has been proved, the same can not as yet be said concerning the infection of man by this species of *Pulex*. Satisfactory experimental proof of the power of any species of flea to communicate plague to man is at present wanting.

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[2] For classification of fleas see *Proc. U. S. N. M.* (1905), **29**, 121–170.

(c) *Ceratophyllus fasciatus* Bosc. This is found on *Mus decumanus* and it is the common flea attacking the rat in Europe. It, like *Ctenocephalus canis* Curtis, has a comb of bristles behind the head and is thus distinguished from *P. cheopis* Rothsch.

(d) *Pulex irritans* Linn. or the human flea. This is small and light colored, being found exclusively in dark and dirty houses.

Some curious facts have developed in regard to fleas and their relation to plague. It is a fact that oilmen and dealers in oil never suffer from the infection. Not a single oilman was included among the million who died of plague in Egypt in 1897. Lingi of Pavia records that during twenty-seven years while he was attendant at the pesthouse in Smyrna, he found friction with oil more efficacious than any other medicine as a prophylactic against this disease. In this connection Capt. Ziston, I. M. S., states:

> "Can the relative immunity of Calcutta and Madras compared with Bombay and the Punjab be due to the habit of daily anointing the body with oil in the two former presidencies?"

It is also notorious that in India visits at night to plague-infected houses have frequently been followed by fatal results, while the same dwellings could be entered with impunity during the day.

We are now waging war in Hongkong against fleas, the object being as far as possible to kill the ova. When the cleansing work is completed by the tenants, the inspector visits every floor, accompanied by the foreman interpreter and some of the coolies, with a bucket of *liquid fuel* (pesterine) and some mops, and this is applied to the sides and corners of the floors, and the skirtings and around the partitions of the cubicles. In other districts phenol is being used in the same away as a pulicide.

The tenants also are invited to have their bedding, clothing, etc., disinfected by steam. By these means it is hoped to destroy the fleas, and it will be interesting to see what effect these measures will have on incidence of plague this year in Hongkong.

During the dry winter season fleas are remarkably scarce, therefore, this investigation will be continued during the hot, damp months.

RATS ENCOUNTERED IN HONGKONG.

(a) *Mus rattus* Linn., the black or ship rat. The most common color of this animal is a dirty gray. The tail is longer than the head and body together, is generally slender and tapers to a fine point. The ears are moderately large, standing up distinct out of the fur and extending to the eye and even beyond it when laid forward. The animal frequents roofs of houses and even trees.

(b) *Mus decumanus* Pallas., the brown rat, also called the Norway or domestic rat. It is a large rat which in European countries has gradually displaced *Mus rattus.* It is a burrowing animal and frequents drains and cellars. There is a little to choose in color between this and the black variety. The brown rat is grayer and of a lighter shade, and this color is more noticeable when a number of the two species are examined together. The tail is shorter than the head and body together, and ends in a blunt point. The ears are short.

(c) ***Mus musculus*** Linn., the common mouse. This resembles ***M. rattus*** rather than *M. decumanus.*

(d) *Sorex giganteus* Is. Geoffr., the musk rat or musk shrew. This is neither a rat proper nor a rodent, but belongs to the insectivora. Its outline closely resembles that of a rat, but it is appreciably smaller than ***M. rattus.*** It is distinguished by its overpowering, musky odor.

There are also hybrid varieties, presenting the long ears of ***Mus rattus*** and the short, coarse tail of *decumanus,* the typical characteristics of the different species being only attained by the adult male.

The following roughly gives the percentages of the different species of rats met with in Hongkong:

	Per cent.
Black rats, ***Muss rattus***	12
Brown rats, ***Mus decumanus***	18
Mice, ***Mus musculus***	48
Sorex giganteus	2
Hybrid rats, size of ***M. rattus***	5
Undetermined rats	15

TABLE I.—*Showing the number of cases of plague known to have occurred in the colony each month from 1895 to 1904.*

Month.	1895.	1896.	1897.	1898.	1899.	1900.	1901.	1902.	1903.	1904.
January		49		9	1	8	7	1	4	
February		125		67	2	8	14	1	29	3
March		168		137	25	5	54	2	115	4
April	3	316		468	101	94	160	27	272	40
May	2	344	3	534	421	326	701	157	515	185
June	13	113	1	92	514	325	551	194	343	194
July	2	52	11	7	263	209	109	131	85	96
August	4	25	1	2	86	80	27	50	32	19
September	3	9	1	1	57	16	24	2	9	9
October		2		2	4	12	1	2	5	Nil.
November	5	1	2		1	2	1	1	4	5
December	12		2	1	11	2	2	4	2	5
Total	44	1,204	21	1,320	1,486	1,087	1,651	572	1,415	510

AN INVESTIGATION OF THE QUANTITATIVE RELATIONSHIPS BETWEEN AGGLUTININ, AGGLUTINOID AND AGGLUTINABLE SUBSTANCE.

By Y. K. Ohno.[1]

(From the Serum Division, Biological Laboratory, Bureau of Science, Manila, P. I.)

This article is a summary of an extensive piece of experimental work conducted for the last two years as a continuation of previous studies entitled "Equation of Curves and the Agglutination Phenomenon" (read before the Annual Meeting of the Association for Medical Research, March 24, 1905), and "The Relation between Agglutinin and Bacteriolysin" (read before the Section of Bacteriology, Hygiene and Infectious Diseases, Japanese Medical Congress, Tokyo, March 4, 1906). After numerous preliminary studies the attempt was made to determine the law governing the mechanism of agglutination by the employment of physico-chemical methods, and formulæ were established which expressed with exactness the quantitative reactions occurring between agglutinin, agglutinoid and agglutinable substance.

The preliminary studies established an exact technique. A bacterial suspension was used of which the dose constantly employed, (0.5 cubic centimeter) contained 0.5 milligram of bacteria by weight. Each test tube in every experiment contained a constant volume of 2 cubic centimeters.[2] The bacterial emulsion was made from 24-hour agar slant cultures killed by the addition of 1 per cent formalin. It was found that the dead cultures registered more exactly the limits of agglutination than living ones. The experiments were performed with *B. typhosus*, *B. dysenteriæ*, *B. paratyphosus*, *B. coli*, *B. pyocyaneus*, *V. choleræ*, *Meningococcus intracellularis*, and *Staphylococcus pyogenes aureus*, together with corresponding immune sera. In performing the agglutination experiments the various dilutions were prepared, placed in the incubator at 37° C. and allowed to stand for twenty-four hours. The macroscopic method was uniformly employed. Each one of the procedures mentioned above was adopted after critical study and experimentation and further studies were made to ascertain the optimum quantity and concentration of salt solution.

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[1] Read at the Fourth Annual Meeting of the Philippine Islands Medical Association at Manila, P. I., on March 2, 1907.

[2] Which each test tube contains 0.5 milligram of bacteria.

In standardizing the units, a unit of agglutinin (or agglutinoid) was selected as that amount which is contained in a quantity of serum sufficient to agglutinate completely 1 milligram of bacterial culture suspended in 0.85 per cent salt solution when the experiment is conducted for twenty-four hours at 37° C. Complete agglutination was defined as that reaction which results in sedimentation of all particles with clearing of the fluid. For the purposes of experiment it is assumed that one unit of agglutinin will always combine with a certain fixed amount of agglutinable substance. Having established a definite and exact technique by these studies and having critically reviewed similar studies of Joos, Eisenberg and Folk and others, experiments follow which are used in the elaboration of formulæ representing the values of agglutinin A and agglutinoid B in 1 cubic centimeter of agglutinating serum. The formulæ established are as follows:

$$A = \frac{CM(G-m)}{M-m}$$

$$B = \frac{Cm(M-G)}{M-m}$$

$$\frac{1}{X} = \frac{G-m}{M-m}$$

In these equations:

A = the number of agglutinin units (Ag) contained in 1 cubic centimeter of serum tested.

B = the number of agglutinoid units (Ao) contained in 1 cubic centimeter of serum.

C = the weight in milligrams of the agglutinable substance contained in each tube, namely the weight contained in 0.5 milligram of bacteria.

$\frac{1}{G}$ = the highest serum dilution in which complete agglutination occurs.

$\frac{1}{m}$ = the serum dilution just too low to cause a visible agglutination but still causing invisible agglutination.

$\frac{1}{M}$ = the serum dilution just too high to cause visible agglutination but still causing invisible agglutination.

$\frac{C}{X}$ = the quantity of substance agglutinated at a serum dilution of $\frac{1}{m}$ or $\frac{1}{M}$.

The correctness of the above equations was established by proving through them the following propositions:

1. The value of X must always be the same with the same bacterial culture, notwithstanding all modifications which may occur in the serum.

2. The value of A and of B must be constant or nearly so, even if we vary the value of C within limits which do not cause X to change.[3]
3. The quantity of bacterial culture uniting with agglutinin at any particular degree of reaction can be established and remains about the same, when we use the same bacterial suspension, notwithstanding all modifications which may occur in the serum.
4. Having determined the quantities of bacterial culture uniting with agglutinin in the different grades of reaction, the value of "m" can be calculated from the known amount of agglutinated substance concerned in the antephase of $\frac{1}{D}$ dilution of the serum.[4]
5. In the same way the value of M can be calculated from the known value of agglutinated substance concerned in the postphase at $\frac{1}{D}$ dilution of the serum.
6. The value of G can be calculated from the known value of agglutinated substance at $\frac{1}{D}$ dilution in the antephase of $\frac{1}{M}$.

The failure of other investigators in their attempts to find the law governing the agglutination phenomena and to express it in a mathematical equation, proceeds in part either from their selection of standards of measurement which are not sufficiently accurate, or from their adoption of unsuitable units, or, as in the cases of Eisenberg and Volk and Craw and Joos, from their allowing too short a time for complete agglutination to occur. The preliminary steps which led to my discovering the formula for agglutination were, first, my assumption that agglutinin, agglutinoid and agglutinable substance always unite according to a fixed ratio; second my adoption of suitable units; third, my adoption of a scale expressing the degrees of agglutination with a fair degree of accuracy; fourth, my assumption that agglutinoid is present to some extent in every agglutinating serum; and fifth, my assumption that every reaction of agglutination is accompanied by a certain amount of invisible agglutination.

As the result of their studies, Eisenberg and Volk insist that the combining ratio of agglutinin and agglutinable substance varies according to the quantities employed and they express this fact by means of their "coëfficient of absorption." My investigations lead to the conclusion that these experimentors have three constant errors in their experiments, first, their neglect of agglutinoid; second, *their failure to take into account the degeneration of agglutinin, produced by the temperature during the agglutination test;* and third, *their failure to appreciate the difference between the quantity of united (fixed) agglutinin and that of agglutinated agglutinin.*

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[3] If the value of C is too high or too low, the density of the bacterial emulsion in the test tube is so much changed that it is not possible to determine exactly the point represented by $\frac{C}{X}$.

[4] $\frac{1}{D}$ = the degree of dilution of the agglutinating serum in any one given test tube.

In the antephase of agglutination, the serum, even though it contain a great quantity of agglutinin, can agglutinate only that quantity of agglutinable substance which is not picked up by agglutinoid, as the latter unites more readily than agglutinin with agglutinable substance; therefore, the proportions of agglutinin uniting with agglutinable substance during the antephase do not show the usual regular proportions. However, the regular ratio between agglutinoid and agglutinable substance can be shown by subtracting the available agglutinable substance, as indicated by the degree of agglutination, from the amount of agglutinable substance introduced into the test tube. The variations in the quantity of agglutinable substance united with agglutinin at different serum dilutions is, therefore, not a proof of different grades of absorption as Eisenberg and Volk consider it to be, but is dependent upon the presence of agglutinoid.

The rate of conversion of agglutinin to agglutinoid varies with the temperature and the dilution at which the agglutination test is performed, being greater at a high temperature and in high dilution. Eisenberg and Volk did not pay attention to this fact, although it is of importance in considering a theory of agglutination.

I accept the view first advanced by Bordet that agglutination may be divided into a stage of fixation of agglutinin by bacilli, and a stage of aggregation of bacilli united with agglutinin. However, according to the results of my experiments, three and one-half to four and one-half hours at 37° C. or four and one-half to five and one-half hours at room temperature (first two hours at 37° C.) is necessary for the fixation of agglutinin to bacilli. The time required for aggregation is much longer than that needed for fixation, and if we do not allow sufficient time for aggregation to affect all the quantity of fixed agglutinable substance, we will not be able to form an accurate idea of the degree of agglutination produced by any given amount of serum. My experiments indicate that it requires the time limits given above for a complete union and from twenty to twenty-four hours at 37° C. for complete aggregation. As Eisenberg and Volk conducted their tests for only two hours at 37° C. followed by twenty-two hours at room temperature, I estimate that they recognized only three-fifths of the real value of their serum; therefore, the quantity of absorbed agglutinin, calculated by Eisenberg and Volk, is larger than the real quantity by a certain amount of agglutinin and agglutinoid, which is to be given by the expression:

$$\left(\tfrac{2}{5}\, r' + d'\right)\ \mathrm{AgE} - \mathrm{AgD}$$

Where r' = the quantity of agglutinin remaining ununited;

d' = number of units of agglutinin degenerating during the test; and AgE and AgD represent respectively the agglutinin and agglutinoid units of Eisenberg and Volk.

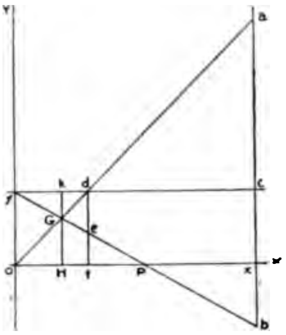
From this equation we observe a third source of error in Eisenberg and Volk's method of obtaining their "coefficient of absorption."

After correcting the errors just pointed out, a repetition of the experiments performed according to the method of Eisenberg and Volk gives values agreeing entirely with those calculated and this also substantiates the truth of my assumptions and formulæ.

The curves graphically representing the phenomenon of agglutination (see fig. 1) are two straight lines ($x - y = 0$ and $\frac{B}{A}x + y - C = 0$) which interact with each other and fulfill the equation.

$$Bx^2 + Axy - ACx + ACy - Bxy - Ay^2 = 0$$

where x is the function of the quantity of serum and y that of the degree of agglutination (that is, the quantity of agglutinable substance agglutinated) within the limits of $x = \frac{AC}{B}$ and $y = \frac{AB}{A+B}$, i. e., within the limits of the agglutinative power of a serum which contains A of agglutinin unit (Ag) and B of agglutinoid unit (Ao) in 1 cubic centimeter, C being the quantity of bacterial culture in each test tube.



$Ox = ax = A$
$Oy = cx = C$
$bx + cx = B$
The equation for the curve O G P is $Bx^2 + Axy - ACx + ACy - Bxy - Ay^2 = 0$

FIG. 1

The serum is also represented by a straight line ao (see fig. 2) the formula of which is $y = \frac{B}{A}x$. The limit of agglutination is ωa, ω being the center of coördinates and a having an ordinate $\frac{1}{2}$ Ao (agglutinoid unit), while at the point e which has an abscissa $\frac{1}{2}\left(\frac{A}{A+B}\right)$ the phenomenon is most complete. The limit of the quantity of agglutinoid which causes the disappearance of agglutination (in the macroscopical test) is A (X — 1), where the value of X varies according to the kind of bacilli, while the relation between the quantities of agglutinin and agglutinoid required to keep complete agglutination with some degree of serum dilution, while both substances are variable, is $\frac{A}{B} > \frac{f}{C-f}$, where f is the quantity of agglutinated agglutinable substance which varies according to the different species of bacilli.

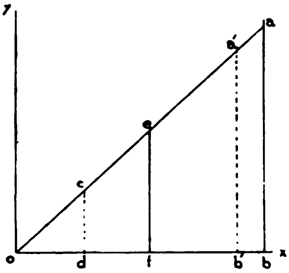


FIG. 2.

Serum has a coefficient of viscosity about 300 times greater than that of salt solution. This great viscosity causes the depression of the phenomena of agglutination. The grade of depression, plotted in the coördinate system, is approximately expressed by the formula,

$$y^2=4\ Kx.$$

the equation of a parabolic curve, where y is the degree of depression; x the quantity of serum in the test tube, and K is a constant, which varies according to the type of serum as follows:

K	with the serum of
206.5	rabbit
233.5	calf
345.8	horse
367.0	cow

where $y=100$ (to express the percentage of depression of agglutination with a certain quantity of united agglutinin) and $x=1$ (taking 2 cubic centimeters of serum in a test tube as the unit). In consideration of this fact, it seems that we need to correct the values of agglutinin and agglutinoid from the formula

$$A = CM\frac{G-m}{M-m}$$

$$B = Cm\frac{M-G}{M-m}$$

because the value of m is somewhat smaller than it should be, but practically we need not make such a correction because the difference is so very slight that we can neglect it in calculation, it (δ) being expressed by the equation

$$\delta=\frac{1}{50}\sqrt{KD}$$

where D is the reciprocal of serum dilution $\frac{1}{D}$, while the value of K varies from 14 to 20. Therefore, the value of δ is approximately 0.84, at the maximum, when $M=10$. When $M=10{,}000$ the value of δ is 0.004 and so on. In estimating the *grade of agglutination*, on the other hand, we must correct by adding the difference, because this quantity is greatly influenced by even such a slight amount. When we correct the quantity of united agglutinin by adding the difference, we obtain agreement between the calculated grades of agglutination *in both ante- and post-phase*, in cases in which the same quantity of agglutinin is united and this supports the theory that agglutinin always combines with agglutinable substance in a constant ratio and demonstrates the influence of serum viscosity upon agglutination.

While at the post-phase of agglutination the total quantity of agglutinin is absorbed (united) by the agglutinable substance, during the antephase only those units of agglutinable substance which remain united with agglutinoid can absorb equal units of agglutinin; that is:

$$\text{"quantity of combined agglutinin"} = \mathrm{C}\ (\text{units of agglutinable substance}) - \frac{\mathrm{B}}{\mathrm{D}}$$

while

$$\text{"quantity of free remaining agglutinin"} = \frac{\mathrm{A}}{\mathrm{D}} - \text{"quantity of combined agglutinin"}$$

$$= \frac{\mathrm{A}}{\mathrm{D}} - \left(\mathrm{C} - \frac{\mathrm{B}}{\mathrm{D}}\right)$$

where $\frac{1}{\mathrm{D}}$ is the grade of dilution and $\frac{\mathrm{B}}{\mathrm{D}}$ must be within the limits of $\mathrm{C} = \frac{\mathrm{B}}{\mathrm{D}}$. From these equations it needs no proof that Arrhenius' formula is not correct, because according to his formula:

$$\frac{(\text{quantity of absorbed agglutinin})^3}{(\text{quantity of free-remained agglutinin})^2} = \mathrm{k}$$

that is:

$$\frac{\left(\mathrm{C} - \frac{\mathrm{B}}{\mathrm{D}}\right)^3}{\left(\frac{\mathrm{A}}{\mathrm{D}} - \mathrm{C} + \frac{\mathrm{B}}{\mathrm{D}}\right)^2} = \mathrm{k}^1$$

which is impossible *when D and C are variable,* even with any values of C and D.

The degeneration of one unit of agglutinin will not always lead to the production of one unit of agglutinoid. In many cases the agglutinin degenerates even more completely, the uniting group being destroyed as well as the functioning group. Thus the conversion of agglutinin into agglutinoid is irregular both in regard to rate and amount. The destruction of agglutinophore groups is greater on the addition of alkali than of acid, while formalin does not affect the serum so seriously. From the results of my experiments we see that the irregular production of agglutinoid by the degeneration of agglutinin is not due to a difference between the haptophore groups of agglutinin and agglutinoid, but to the degree of destruction of the haptophorous groups of agglutinin, brought about by chemical or physical factors. We also secure a similar irregularity in the production of agglutinoid in the blood of animals.

The results of experiments show us that the quantity of agglutinoid production is not in a constant ratio to the degeneration of agglutinin. The cause is to be found in the irregularity of agglutinin production and in some forces which are able to destroy not only hemiagglutinin, but also haptophore groups.

If a serum contains two different kinds of agglutinin A and A′, and their respective agglutinoids B and B′, the haptophore groups of A and

B being entirely distinct from that of A′ and B′, and if the quantities of A and A′ and also those of B and B′ are not equal, then the curve graphically representing the agglutination phenomena of such a serum is composed of four straight lines intersecting at three points and having two apices like a mountain with two peaks. Such a serum can be termed "poly-apical," in contradistinction to one having only one apex, which would consequently be called a "mono-apex-serum." With the former it is difficult to estimate the value of agglutinin and agglutinoid from the formula

$$A = CM \frac{G - m}{M - m}$$

$$B = Cm \frac{M - G}{M - m}$$

with known values of m, G, and M, because there are two factors for G. For this reason *I have used only mono-apex-serum, either obtained as such directly from animals or man or by a modification of a poly-apical variety.* It is very interesting to discuss the character of poly-apical sera, but their consideration depends rather upon the relations between the bacterial receptors and amboceptors, and consequently I will leave this topic for another paper which will be especially devoted to this problem.

At the result of this series of experiments I am of the opinion that the union of agglutinin and agglutinable substance is not analogous to the fixation of dye by a tissue, as Bordet considers it to be, but I believe it to be a chemical reaction, as is maintained by Ehrlich.

The detailed report, of which this is a summary, will shortly be published in another journal.

PECULIAR CASES OF TRAUMATISM OF INTERNAL ORGANS, SOME DUE TO TROPICAL CONDITIONS AND PRACTICES.

By Maximilian Herzog.

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

During the years 1904 and 1905, I encountered among my autopsy material five cases of fatal traumatism of internal organs without external injuries. However, in two of these five instances fractured ribs were responsible for the internal damage, which was followed by fatal hæmorrhage. Each one of the five presents quite peculiar and noteworthy features, two are probably unique in kind; two were of rupture of the spleen occurring in splenomegaly, two of rupure of the heart, one a fatty heart which, in the absence of any other injury, was pierced by a rib in consequence of a slight fall, and one case, rupture of fatty liver, occurred during parturition because of native obstetrical practice.

TWO CASES OF SPLEEN RUPTURE IN SPLENOMEGALY.

Rupture of the spleen in the tropics is probably not at all rare, although heretofore, it appears to have been the general impression that it is so.

Glogner[1] has quite recently called attention to its occurrence in Java, where, during the years 1893 to 1898 he saw ten cases of rupture of the spleen. A summary of Glogner's observations will be of interest. In all ten cases, the spleen was enlarged, in several instances very much so; in all, the cause of the rupture, followed by fatal hæmorrhage, was comparatively slight; in four cases malarial parasites were found in the spleen upon post-mortem examination. Glogner, from his observations, draws the practical conclusion that a person during or after a malarial infection, as long as an enlarged spleen is present, should be guarded carefully against any danger which might lead to a rupture of the spleen.

Our own two cases of rupture of the spleen are the following:

Case I.—J. R., a 15-year old, male, Filipino boy, on July 15, 1904, was brought to the San Juan de Dios Hospital. It appears that the boy had received a slight kick or had suffered a fall. No diagnosis was made and he died syncope on July 16, in the afternoon.

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[1] Glogner: Ueber Milzrupturen in den Tropen. *Arch. f. Schiffs u. Trop. Hyg.* (1906), 10, 17.

Necropsy (*No. 1003*).—Post-mortem examination made July 17, 1904, at 10 a. m., fifteen hours after death. Body of a well-developed young male native. Post-mortem rigidity still quite well marked. Post mortem lividity very moderate. The whole surface, particularly the mucous membranes, is very pale and anæmic. The abdomen appears much distended, particularly the upper part. There are no signs of external violence, and no wounds or abrasions. On opening the abdomen very extensive blood coagula are found to fill every available space below the diaphragm. Serum has collected in the dependent parts of the abdominal cavity, and the mass of serum and coagula removed amounts to about two to three liters. All the organs are found to be very anæmic. The heart is soft and flabby, but otherwise normal. The lungs are rather collapsed and pale pink in color. Both of them have formed some adhesions and the apex of the right lung contains four caseous nodules, varying in size from a pea to a hazelnut. Otherwise, the lungs, the trachea, the bronchi and the larynx are normal. The spleen is very soft, flabby and friable, measuring 23 by 10 by 6½ centimeters and weighing 655 grams. The capsule is wrinkled, transparent and grayish-blue. The veins entering the hilum are very much enlarged and have very thin walls. On the posterior, lateral surface of the spleen—namely, that which was in contact with the internal thoracic wall of the left side—there is found a rupture, which extends from the outer lateral margin of the organ toward the hilum. The rupture is about 6 centimeters long and is directed somewhat downwards. It forms a triangular gap, the base of which is found at the hilum, being 2½ centimeters long. The rupture has torn into some of the larger branches of the splenic vein. The lesser omentum contains a small, round body of the size of a hazelnut, which is either an accessory spleen or a hæmolymph gland. On inspecting the internal wall of the thoracic cavity, it is found that the 9th rib of the left side is fractured. This fracture is situated 9.5 centimeters behind the anterior end of the rib. It is an incomplete, green-stick fracture, and is situated in the mid-axillary line. The anterior segment of the fracture is very sharply pointed. It projects somewhat into the pleura costalis. The region around this fracture, for a radius of several centimeters, is hæmorrhagic. It is clear that this fracture must have been produced by a dull force, which, however, left no sign on the integument; it was probably a force exerted very quickly, not crushing the soft parts, but splitting the rib and driving the anterior fragment into the exceedingly soft, friable, enlarged spleen and producing a rupture. The kidneys are normal. The adrenals are normal. The capsule of the liver is smooth and transparent, and in color pale pinkish-blue, the upper surface showing a number of small, punctiform hæmorrhages. On the cut surface the organ appears brownish-pink. The gall-bladder is normal. The ducts are normal. The mucosa of the duodenum and stomach is pale. The small intestine, the large intestine, the prostate, etc., are normal. The brain and cord are normal.

Anatomical diagnosis.—Splenomegaly (primary ?), fracture of the ninth rib of the left side, rupture of the spleen, hæmorrhage, general anæmia of all the internal organs, tuberculosis of the apex of the right lung. No malarial parasites were found in smears prepared from the spleen.

CASE II.—M. V., 25 years old, was working on a new building on February 13, 1905. He was engaged in lifting, by means of a lever, certain heavy weights, and just as he had brought the lever to the required elevation, he staggered and fell to the ground. His friends applied "smelling salts," thinking that he had fainted, but as he did not respond to this treatment, the Bureau of Health was notified. The time between the injury and his death was probably about twenty minutes. His wife stated that his health had not varied since she had known him. The post-mortem examination (Necropsy No. 1108) was made two hours after death. The findings were: Beginning cirrhosis of the liver, splenomegaly (very large spleen), rupture of the spleen, copious hæmorrhage into the abdominal cavity. No external injuries, no ribs fractured. Smears from the spleen showed neither malarial parasites nor the Donovan-Leishmann bodies.

PERFORATION OF THE HEART.

The two following descriptions refer to cases of perforation of the heart. In one of them the myocardium' was ruptured by a fractured rib, *but not the pericardium* and the victim did not die from the effects of losing a large amount of blood, but from compression of the heart and cessation of its action. In the second case a floating rib perforated a heart which was in an advanced condition of fatty degeneration.

CASE III.—Necropsy No. 1004. Sra. M. R., Filipina, age, 25, died July 17, 1904. The post-mortem examination was made July 18, twelve hourse after death. Immediate cause of death not known. It was stated that she had been struck by a carromata shortly before she died. Body of a well-developed, young, native woman, 25 to 30 years of age. Post-mortem rigidity strongly marked. Post-mortem lividity quite noticeable. Abdomen somewhat distended. A repeated careful inspection fails to show any signs of external violence. No wounds, contusions or abrasions of any kind to be seen. On opening the thoracic cavity, the pericardium is found to be much distended, and shining through it there appears to be a firm, dark, blood coagulum. On opening the pericardium it is found to contain a large amount of dark, coagulated, gelatinous blood and blood-tinged serum, distending the pericardium *ad maximum* and compressing the heart. A careful examination fails to show any perforation in the pericardium. The heart, which weighs about 226 grams, presents a perforation, which begins 2 centimeters to the left of the anterior border of the interventricular septum. The perforation extends almost horizontally toward the left, being a little downwardly inclined. It forms a slit 2.2 centimeters long, running 5 centimeters above the apex and 5.5 centimeters below the sulcus of the heart. The edges of the perforation are almost clean-cut where they enter the myocardium, as if they had been produced by a dull, somewhat serrated knife. The cut takes a somewhat downward and inward course, traveling through the whole thickness of the myocardium. Where the cut enters the cavity of the heart, the margins are not very smooth, but rather irregular and ragged. The consistensy of the myocardium is good. Its color is pinkish-brown and all the serous surfaces are smooth. There are no atheromatous changes. The heart is covered with a very moderate amount of epicardial fat. In short, the whole organ is absolutely normal. After the removal of the lungs (the apex of the right one showing a very few tubercles and a little caseous nodule not larger than a lentil) it is seen that the second, fourth and fifth ribs are fractured. The fracture of the second rib is found to be 7.5 centimeters posterior to the sternal articulation, that of the fourth one 9 and that of the fifth one 9.5 centimeters. The anterior fragments are directed inwards. The fragments of the fourth and fifth ribs are very sharp and are surrounded by an area or subpleural blood extravasation. However, these fragments have not perforated the pleura costalis. The extravasated blood is strictly subpleural and no free blood is found on the surface on the pleura. The uterus appears somewhat enlarged and the left ovary shows a fresh, but already closed corpus lutem. On opening the uterine cavity, a little hæmorrhagic mass, about one-half centimeter in diameter, is found embedded in the mucosa of the posterior wall, near the entrance of the left tube.

All the organs of the body, with the exception of the apex of the right lung are found to be absolutely normal. They are all more or less congested with dark, fluid blood. It appears clear that the woman must have been struck at the side of her body or in the back by a swiftly moving force. This force, however, did not produce any signs of external violence, particularly no contusions, abrasions or wounds. The force traveled through the soft parts, and meeting the resistance of the ribs, fractured them. The anterior, sharp fragment of the fourth or of the fifth rib was evidently driven into the wall of the left ventricle, producing a complete perforation. A highly interesting point is that the sharp fragments neither perforated the pleura costalis nor the parietal layer of the pericardium.

Only when the resistance of the firm wall of the ventricle was encountered, did a rupture or perforation occur, a hæmorrhage taking place, and when the pericardium was completely filled and the myocardium much compressed, the heart's action came to a sudden standstill. Death occurred from syncope.

Anatomical diagnosis.—Fracture of the second, fourth and fifth ribs of the left side. Complete perforation of the wall of the left ventricle. Hæmorrhage into the pericardium. Compression of the myocardium. Beginning tuberculosis of the apex of the right lung.

Microscopic examination of the myocardium showed it to be perfectly normal.

CASE IV.—Necropsy No. 1185, May 15, 1905. A. R., 70 years old, female Filipina, died May 13, 1905, at 3 p. m. Post-mortem examination forty-two hours after death. This woman fell downstairs. She immediately went into collapse and died within fifteen minutes after the accident.

Body of a medium-sized, quite fat woman, probably younger than 70 years old, perhaps 60. Post-mortem rigidity has disappeared, post-mortem lividity well marked and extensive over the dependent parts of the body. Putrefactive changes well advanced. A close inspection fails to show any signs of external violence; there are no signs of a contusion, the skin shows no areas of suggilation. On opening the body, the abdominal cavity presents nothing abnormal. However, in the thoracic cavity, the pericardium is found distended and it contains a soft blood coagulum and hæmorrhagic, dirty-brown fluid. A blood coagulum of the size of two fists is also found in the right pleural cavity. The anterior surface of the pericardium presents a slit 18 millimeters long. Its direction is from above downward, its margins are sharp cut, linear on the whole, but here and there irregular and wavy, however, not serrated or fringed. Corresponding to this slit in the pericardium there is a perforation in the anterior wall of the right ventricle. It is almost immediately to the right of the interventricular septum and 8.5 centimeters above the apex of the heart. It is 7 millimeters long but not clean cut, rather irregular and with ragged margins. Its direction is oblique, being from above and to the left, to below and to the right. The perforation traverses the whole of the myocardium which is here less than 2 millimeters thick. The exit of the perforation into the endocardium is about one-half the size of its entrance at the outer surface of the myocardium. The heart as a whole is somewhat enlarged in its diameters; it measures from base to apex 13.5 centimeters; 9 centimeters across the broadest point, and it is 7 centimeters thick. It weighs, including the arch of the aorta, 380 grams. The walls of the left ventricle are thickened, but the myocardium here, as elsewhere, is very friable, flabby and soft and of a grayish-yellowish, dirty-pink color; it is porous and honeycombed, but this condition is evidently due to the action of gas forming bacilli and must be looked upon as a post-mortem change. The right ventricle is dilated; its wall, particularly the anterior part, is very thin, measuring on an average only 2 to 3 millimeters in thickness. The endocardium is smooth, the valves show no change, but the right auriculo-ventricular opening is enlarged. The whole arch of the aorta is atheromatous and the intima covered with calcareous patches; the coronaries are likewise atheromatous. The lungs are normal. The osseous framework of the thorax is normal, none of the ribs are broken, but both of the tenth ribs are unusually long and their free, floating ends reach very much forward. The tissues over the free end of the tenth rib of the right side are decidedly hyperæmic, however, there is no break of continuity in this region. The spleen is very small, soft and mushy. The kidneys are small, slightly uneven, the capsules peel off with some difficulty. Other abdominal organs, normal; putrefactive changes well advanced. The brain is of medium size (weight, 1,210 grams), all the arteries at the base are in an advanced stage of atheromatosis.

Anatomical diagnosis.—Hypertrophy with concentric atrophy, fatty degeneration, and dilatation of the myocardium. Perforation of the myocardium and of the atrophic anterior wall of the right ventricle; hæmorrhage into the pericardium and into the left pleural cavity. Extensive atheromatosis of the aorta, of the coronary arteries and of all the vessels at the base of the brain. Atrophic interstitial nephritis of moderate degree. Abnormal lenght of both of the tenth ribs.

Epicrisis.—It is evident that in consequence of the fall, the free end of an unusually long tenth rib which reached far forward perforated the pericardium and the atrophic, degenerated myocardium, and this led to the hæmorrhage which became fatal inside of a short time after the accident had happened.

RUPTURE OF THE LIVER DUE TO AN OBSTETRICAL PRACTICE IN THE PHILIPPINE ISLANDS.

It is a well-known fact that certain races have adopted peculiar practices to assist a parturient woman during labor, in order to facilitate and hasten the expulsion of the child from the uterus. The North-American Indians, for instance, place a woman in labor with her back against a tree, an old woman then stands behind the tree, reaches around the latter as well as the woman propped up against it, and makes violent compression over her abdominal region. The native Filipinos have a method which, while different in arrangement, is based upon the same principle. They place a folded piece of cloth, a long towel, or some similar thing above the bony pelvis and around the loins of the woman in labor, and then one or two persons with all their might make traction on the encircling bandage. That this method may, under special circumstances, lead to much harm, in fact to a fatal issue, is shown by the following case. Nothing is known concerning its clinical history, except that one of the medical inspectors of the Bureau of Health was called in February, 1906, to view the remains of a woman who had died quite suddenly during labor. The body was sent to the morgue, where a post-mortem examination was made. The following were the findings:

CASE V.—Necropsy No. 1661, about twenty hours after death. C., age unknown, a female Filipina, died February 16, 1906, at 1.15 p. m. Cause of death, unknown. Body of a woman, about 35 years old, of medium size and fair nutrition. The woman appears to be pregnant, at or near full term. She appears to be a primipara because the abdominal wall does not present any striæ. There are no external anomalies, but the labium majorum of the left side shows a pediculated fibroma of the size and shape of a large pear. A piece of cloth in the form of a bandage is tied around the upper part of the abdomen, above the umbilicus. This bandage has been drawn so tightly that it has left a deep, annular impression running around the abdomen and back. Post-mortem rigidity has almost disappeared. The post-mortem lividity is well advanced. On cutting through the skin, the tissues are found to be very anæmic and on cutting through the peritoneum the upper part of the abdominal cavity is found to be full of clotted and fluid blood. An examination shows that this hæmorrhage has come from a ruptured liver. Further examination of the internal organs shows the following: The heart is exceedingly soft and flabby, grayish-yellow in color. The spleen is small, soft and friable, otherwise normal. Both kidneys show signs of fatty and parenchymatous degeneration. The liver is large, somewhat swollen, weighs 2,280 grams, is pale-yellow in color, exceedingly soft and flabby and so friable that on handling it a rupture is produced on the upper surface of the left lobe. The upper surface of the right lobe presents two deep, lacerated perforations and the tissues here are suggilated with extravasated blood. It was at this place that clots of blood were found; on opening the abdomen, they needed to be removed in order to show the condition of the liver. Examination of the region of the liver and of the right thorax shows the ruptures in the liver to have been produced by the eleventh rib of the right side. It is possible that the outer one of the two perforations has been caused by the twelfth rib. The pleura over the external end of the eleventh rib shows a small area of blood extravasation. It is evident that when this rib was pressed against the liver, perforating the latter, there was enough force used to cause a slight hæmorrhage of the pleura over the end of this rib. The uterus contains a female child nine months old or, at least, near full term in breech presentation. The cervix is soft, somewhat hæmorrhagic and admits two fingers. Evidently, the first stage of labor had begun, but the membranes had not yet ruptured nor had detachment of the placenta taken place. The placenta itself is perfectly normal. All of the other organs including the brain are normal, but they are all profoundly anæmic. The eleventh and twelfth rib were removed and cleaned. The former, the outer end of which presented a sharp point, measured 135 centimeters in length, the latter 9 centimeters.

Microscopic examination of the various organs, pieces of which had been fixed in Zenker's solution and in osmic acid, shows the following: *Liver:* The protoplasm of the parenchyma cells is granular and finely vacuolated, the osmic acid preparations show numerous, small, disk-like, black granules and round, black granules, varying in size from a small coccus to about half the diameter of the cell nuclei. There are also seen black masses of the size of a liver or parenchyma cell and even larger, roundish bodies of this color; these are, of course, all the result of the profound fatty degeneration. The nuclei of the parenchyma cells are generally fairly well stained and many cells show two nuclei. The periportal, interlobular connective tissue shows a slight, but manifest, increase. The *renal* epithelium shows advanced cloudy swelling and fatty degeneration. In the spleen, marked changes are not present, and malarial parasites are not found. The *myocardial* fibers are very indistinctly striated, vacuolated and full of fat granules. The *fibroma of the vulva* is composed of loose, œdematous, fibrous connective tissue; it contains numerous, large vessels; this vascularity had probably developed during the period of gestation.

Anatomical diagnosis.—Fatty degeneration of the heart and of the kidneys and profound fatty degeneration of the liver; perforation of the latter by the eleventh rib, copious hæmorrhage, *uterus gravis menses X.*

The anatomical and histological examination of this case plainly shows that this woman was in the first stage of labor and that she was suffering from a profound fatty degeneration of the liver which may perhaps have been the first stage of acute, yellow atrophy of that organ. When the bandage was applied to assist in labor, as is habitually done among the natives, the force of the pressure was sufficiently great to drive the sharp point of the eleventh rib into a very soft, flabby, fatty liver, thus causing a rupture and fatal hæmorrhage.

THE HABITUAL USE OF OPIUM AS A FACTOR IN THE PRODUCTION OF DISEASES.

By Tee Han Kee.
(From the Bureau of Health, Manila, P. I.)[1]

It is not the intention of this paper to discuss at length the therapeutic use of opium as a medicine, nor is it my desire to treat of the symtomalogy and psychology of the opium habit, for such an attempt would lead away from by main purpose, which is to give an account of the motives of the Chinese in using opium; how they use it, and lastly what are the results, or, in other words, diseases produced by the habit.

Two main reasons could be given as the motives of the Chinese for using opium: 1. For pleasure. 2. As a medicine.

1. *For pleasure.*—After careful inquiry among the Chinese as to their reasons for using opium, the majority of the confirmed consumers will tell us that they began the use of the drug simply for "pleasure," if so it may be termed. The reason the Chinese choose opium may be because it is not so violent a stimulant as alcohol. The force of example and of fashion must also be taken into account in describing the reasons the Chinese have for taking opium. In society, restaurants and public places, opium is almost always offered.

2. *As a medicine.*—The second motive of the Chinese in using opium is due to the widespread popular belief in the medical efficacy of the drug. It has been proved in China that the opium habit, in the majority of cases, dates from the time when the drug was taken for medicinal purposes. In some cases the chronic or recurrent character of the malady necessitates repeated doses; in others the exhilaration and general sense of comfort induced, result in repetition long after the ailment for which the drug was originally taken has passed away. It is a common domestic medicine of the people. It is taken in cases of specific disorders, such as dysentery, rheumatism, tuberculosis, diabetes, and diarrhœa. In malarial and damp tracts there is a general faith in its virtue, either for

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[1] **Read at the Fourth Annual Meeting of the Philippine Medical Association, March 3, 1907.**

warding off or in curing fever. The use of opium as a household remedy has a special importance in a country like China, where the mass of the population is beyond the reach of modern, qualified doctors. Although there are a large number of old-fashioned native practitioners, yet they are only to be found in towns and are chiefly resorted to by persons in easy circumstances; therefore, the poorer sections of the community and especially the agricultural classes, must prescribe for their own ailments. In the country it is used by persons as a restorative and stimulant after they have done hard work or have been much exposed to wet and cold. It is also employed to enable individuals to undergo fatigue on long journeys, and also, on occasions, when special exertion is required. In the large cities the people believe opium to have a special quality as an aphrodisiac.

Enough has now been said concerning the motives of the Chinese in using opium, but before I discuss diseases produced by the habitual use of the drug I wish to say a few words in regard to the modes in which it is consumed.

As a general rule, the commonest and in fact the oldest way, is by smoking. This is done by using a special preparation. This method is employed by the majority of the people, and is the manner in which they find pleasure. In this way the drug is offered to guests on all social occasions. The second, the next most common method is by eating opium. The crude material, the prepared extract, the dried leaves, or more rarely, the patent pills, are used for the purpose. The users either chew the preparation, as is the case with the dried leaves, or they swallow it either as the pills and as the extract, or as morphine. These methods are used by the poorer classes, because they are cheaper and more effective; that is they are generally used by persons who can not afford the luxury of smoking, or who have reached a condition in which smoking no larger satisfies their craving.

The method of hypodermic injection is also used, this is of course of more recent introduction, it is the most harmful and fortunately, the least used. Hydrochloride or sulphate of morphine are generally employed. Hypodermic injections are also habitual with a percentage of individuals of the poorer classes, because comparatively, they are the cheapest of all. Persons who no longer obtain the desired effect by smoking and eating, and those who originally contracted the habit after they first used opium as a medicine to stop pain; or those who desire to have a speedy action of the drug, also employ it. Some individuals have the habit of using all the methods mentioned, that is; smoking, eating and hypodermic injection.

RESULTS OF THE HABITUAL USE OF OPIUM AND THE DISEASES PRODUCED BY IT.

As a rule, confirmed opium consumers owing to the life they lead are predisposed to all varieties of acute or chronic diseases. The narcotic influences which affect the entire system, physically, morally and mentally, act as a sufficiently predisposing factor, but there are many diseases which I believe, are due to the direct action of the opium upon the individual system, although the drug can not be considered as a direct pathogenic cause.

The alimentary canal.—The immediate, specific and remote action of opium on the alimentary canal when the drug is taken per oram is well known. Habitual opium consumers always suffer from dyspepsia. Owing to the action of the drug on the intestines, its consumers are constipated. However, among chronic users of the drug when very large doses are employed, the splanchnic nerves are paralyzed in such degree that diarrhœa (called by the Chinese "opium diarrhœa)" results. This is regarded as a serious and fatal malady, as many persons succumb to it. Opium smokers are always anæmic, partially because the bronchial tubes are continually filled with smoke, with a resultant interference with perfect oxidation. They also suffer from a general, chronic catarrhal condition of the entire respiratory tract, due to the constant and direct irritating action of the smoke on the mucous membrane. The depressing effect of opium on the respiratory centers diminishes the movements of the chest. For these reasons opium users are predisposed to lung troubles and, to judge from my experience in practice, in the greater number of cases the cause of death among these persons is either tuberculosis of the lungs, bronchitis or not uncommonly hypostatic pnéumonia, which is produced by the recumbent position which the consumers always assume. As a whole, without attempting to go into the details, I may say that nearly all the parts of the body are influenced by the use of opium. The brain is usually the chief organ affected, the subject is always drowsy, nervous, weak in character, wanting in energy, and utterly unfit for work. There is a general perversion of the mental faculties, self-control and judgment being weakened. When the craving is satisfied by using the drug, there is a brief period of excitement and exaltation which is generally described as a stimulation, but in reality I do not believe it to be so. In fact, this period consists rather in depression of the sensibility, by which the unfortunate person becomes unconcious of the miseries of his condition, and so accordingly he may be able to perform his duties, and to maintain his appearance better than when deprived of the poison. Melancholia and dementia are not infrequently seen among the habitués of the drug, as a result of its prolonged and continuous use. The hepatic and general metabolism is greatly reduced in activity. Jaundice is often seen. Retention or incontinence of urine, and nocturnal emissions frequently occur. Persons who use hypodermic injections suffer from chronic abscesses appearing in the places where the needle punctures are found. Yawning, a prominent symptom of chronic opium poisoning, often leads to dislocation of the jaw.

Treatment of chronic opium poisoning.—Fully 25 per cent of the Chinese population of this city (6,000 individuals) are confirmed users of one or the other form of opium, and with the present law in effect, and the provision that on and after March 31, 1908, no opium will be imported except for medicinal purposes, our services in attending to the treatment of this chronic poisoning will become more and more necessary. It is true that the treatment of the chronic poisoning offers no very great hope if once a person has contracted the habit. However, in treating these cases it must be remembered that great variations in the intensity of the habit exist among various individuals, and one important point is to discover if the drug is being used as a medicine or for pleasure, for, as a rule, the latter condition is the more amenable to treatment.

There are three principal methods which we may, according to the condition of the patient, employ with fair success.

1. The sanitarium or retreat. 2. The gradual treatment. 3. The bromide or the alcohol treatment.

The first step is to induce the patient to resolve to break up the habit, the determination on the part of the patient himself being very important and absolutely necessary if successful results are to expected. Many cases are encountered in whom the self-control seems completely to have disappeared. However, if the contraction of the habit was due to pleasure and is only recent, determination on the part of the patient alone, together with a prescription of bitters by the physician, will often be sufficient to effect a cure. In these cases the patient is under the impression that the doctor is prescribing for him some medicine to take the place of opium, and he usually is satisfied with whatever he may be given. If restlessness on the part of the habitué is evident, then either the bromide or the alcohol treatment may be administered with fair success, but it must be remembered that bromide and alcohol are cardiac depressants and are to be given with caution, and from my experience, in not too large doses. Many have recommended 120 grains of bromide every two hours, until one ounce or more has been given to produce what is called the "bromide sleep." Others advise the administration of alcohol in such doses as to keep the patient under the influence of alcoholism for several days, when the further treatment is that for ordinary alcoholic excess. Both of these practices are, according to my opinion, impractical and dangerous, as coma and death from syncope frequently occur. If bromide or alcohol is necessary at all, they must be given in small doses, as these remedies are applicable only when the patient has recently acquired the habit. In cases of long standing especially where the habit has been contrated because of an ailment, the immediate removal of the opium often leads to a recurrence of the former disease for which the drug was taken, or it produces such intense misery and depression as really to be dangerous. In such instance the gradual treatment, that is the slow cutting down of the amount consumed, would be more practical and safe. In very bad cases strict observation in an asylum or sanitarium is absolutely necessary.

The treatment of opium habit by such drugs as cocaine and heroine is worse than useless, because the patient merely breaks off one habit to contract another which may be worse.

EDITORIAL.

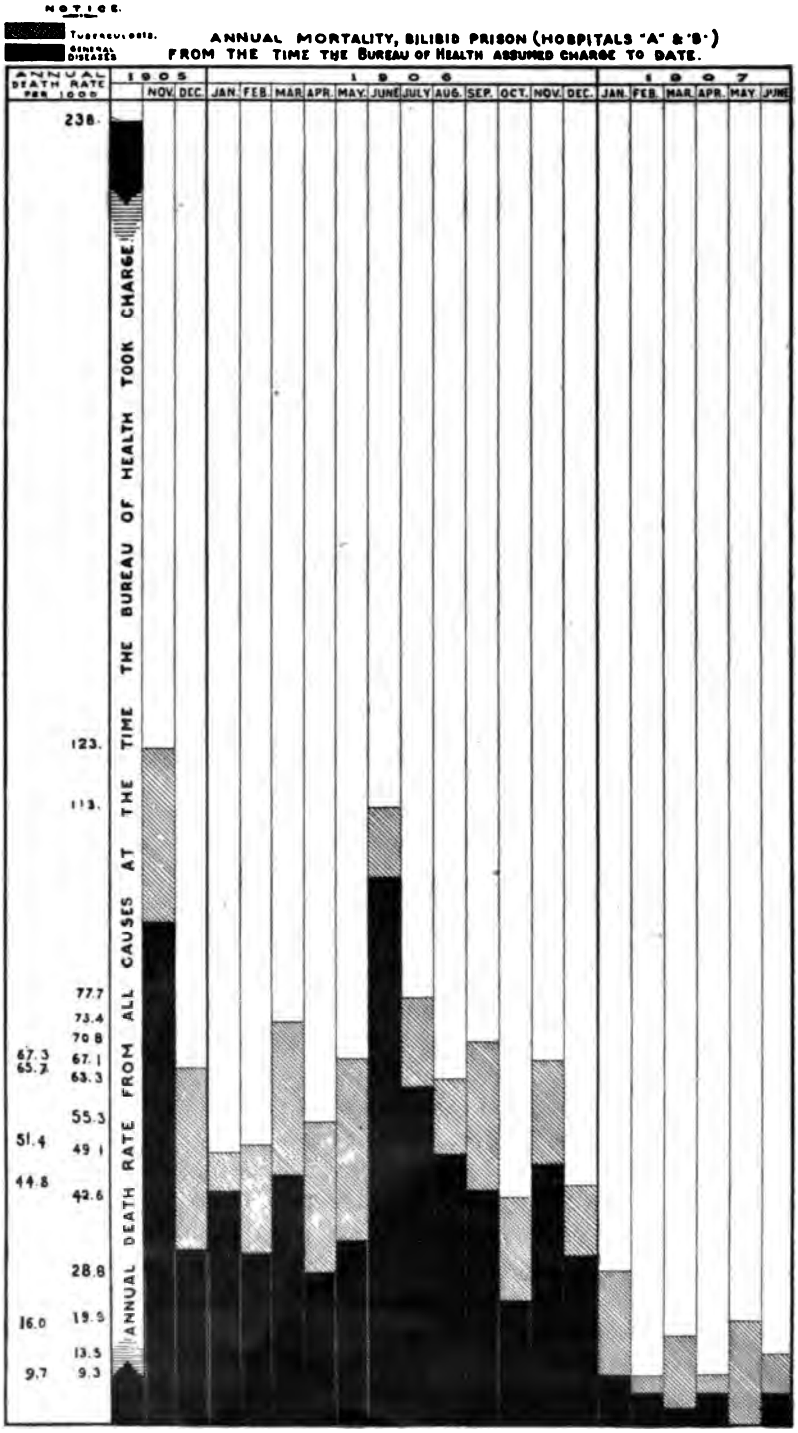
The sanitary and medical work in the Philippine Islands have developed to such an extent that beginning with the Medical Section of Volume III of this JOURNAL, it will be possible to introduce a series of editorials having direct connection, not only with laboratory investigation, but also with the statistical and other results of the medical advances in these Islands. Much material which has gradually accumulated, but which is not of such a nature as to be brought together in formal discussions of research is of the greatest interest to all who are concerned with scientific work in the tropics and it has seemed proper to afford a place in this JOURNAL for the publication of these results. It therefore will be the future policy of this JOURNAL to publish an editorial section of this character in each number of Section B.

PAUL C. FREER.

PROPHYLACTIC MEDICINE AS APPLIED TO THE HYGIENE OF BILIBID PRISON.

Probably one of the most satisfactory results that has ever been achieved by prophylactic medicine is that obtained by the Bureau of Health since the medical work of Bilibid Prison was placed under its charge in November, 1905. The diagram on the following page will show most effectively how the death rate has decreased from 238 per thousand to 13.5 per thousand at the end of June, 1907.

One of the first moves after taking charge was to improve the sanitary condition by admitting light and air and to relieve the overcrowding which was believed to be an important factor in the excessive mortality. A number of structural improvements were made; all the drains were deepened and made semicircular; the level of the ground was raised, and a system of daily sprinkling instituted. Drinking-water barrels were provided with locked covers to guard against contamination. Rigid inspections were made of all latrines. Prisoners who were ill were encouraged to come into the hospital upon the appearance of their first symptoms. Some months after the introduction of these immediate measures, the death rate was reduced to an average of about 75 per thousand, and here it remained; it seemed impossible to lower it further. Like everything else, there was a reason for this. The prisoners were



ANNUAL MORTALITY, BILIBID PRISON (HOSPITALS "A" & "B") FROM THE TIME THE BUREAU OF HEALTH ASSUMED CHARGE TO DATE.

dying with ailments that should not have killed them; their powers of resistance were evidently impaired. The habits and customs of the people with reference to eating immediately suggested a clue and a remedy. The clue pointed to some extraordinary drain on the system. There was plenty of food, but imperfect nourishment. To discover the cause, a routine practice was inaugurated and the fæces of every prisoner in the prison were examined either by members of the staff of the Bureau of Science or by Dr. Shattuck, of the Bureau of Health, for the presence of ova of intestinal parasites; these were found to be present in about 60 per cent of all cases examined. Active therapeutic measures were inaugurated to rid the patients of the causes of these debilitating troubles and the result was immediately satisfactory; the death rate falling below 20 per thousand.

The prevailing diseases treated in Hospital A, Bilibid Prison, were agchylostoma, 1,537 cases; amœbic dysentery, 551 cases; acute dysentery, 174 cases; cholera, 18 cases; pneumonia, 62 cases; beriberi, 60 cases; conjunctivitis, 221 cases, and malaria, 174 cases.

During the previous year only 39 cases of agchylostoma were treated as compared with 1,537 cases during the present year. There have been 551 cases of amœbic dysentery treated as against 111 cases for the preceding year. These figures do not by any means indicate a greater prevalence of this disease and may be explained on the ground that the cases were detected by the systematic stool examinations which have been practiced. Among the rarer parasites that have been found are *Paragonimus westermanii*, 9 cases; *Schistosoma japonicum*, 15 cases: *Opisthorchis sinensis*, 5 cases; *Balantidium coli*, 14 cases; *Tœnia saginata*, 20 cases; *Tœnia solium*, 2 cases; and *Tœnia nana*, 3 cases.

VICTOR G. HEISER.

INTESTINAL PARASITES IN THE PHILIPPINES.

The establishment of a separate department of medical zoölogy in the curriculum of the Philippine Islands Medical School is a step that has been taken to meet in a fundamental and comprehensive manner the seriousness and magnitude of the problem presented by the extreme prevalence of animal parasites among the Filipinos.

The publications of Strong, Musgrave, Shattuck, Cole, Smith, Ashburn, Craig and others have contributed information regarding the species of intestinal worms present in the Islands and the frequency with which certain forms had been encountered, and have served as a basis for the opinion generally prevalent that when the condition become actually known, the population of the Philippines would present one of the most striking instances in the history of medicine of almost universal infection with intestinal worms. With a view to obtaining accurate information concerning the actual percentage of Filipinos infected with animal parasites, the Bureau of Science is at present tabulating the results of the examination of over 4,000 men from the different provinces. While the tabulation is not completed, it has been carried sufficiently far to indicate with fair certainty than not less than 80 per cent of the population of the Islands is infected with one or more species of intestinal worms and that if we consider the different species separately, there is an average of about 200 infections to each 100 of population.

The most comprehensive statistics regarding the prevalence of intestinal worms in tropical countries are those of Dobson and of Fearnside in India, and of the Porto Rican Anæmia Commission. The latter reported about 90 per cent of the population infected and the number of infections with all intestinal worms to be about 140 to each 100 of the population. Fearnside and Dobson each found about 100 infections to 100 people in India.

The relative frequency of different species in the Philippines is not yet definitely determined, further than that hookworms, *Ascaris* and *Trichuris*, are the most prevalent forms and that the first probably infect from 50 to 60 per cent of the total native population. In certain provinces, the ratio of hookworm infection is undoubtedly much higher.

One peculiarity presented by the situation is the fact that while this high proportion of the population shows hookworm infection, severe clinical manifestations of uncinariasis are comparatively rare. While hundreds of cases come annually from the provinces to the hospitals of Manila, exceedingly few, in the absence of malaria and other anæmia-producing diseases, present even mild anæmia, and the infection is discovered in the course of the usual routine stool examinations. Furthermore, careful inquiry among medical men of the Army, Navy, Bureau of Health, and Constabulary, who have served in the provinces, has failed to elicit reports of any remarkable prevalence of anæmia among the people.

Whether or not the explanation of this apparent rarity of clinical symptoms in hookworm infections among the Filipinos is a racial immunity on the part of the people to the toxins secreted by the worms, as has been suggested as the cause of a very similar rarity of symptoms found in negroes, by Stiles in the Southern States and by the Anæmia Commission in Porto Rico, the fact that severe clinical manifestations of uncinariasis are rare in the Philippines materially alters the problem which is presented. Instead of producing an acute condition demanding prompt and radical measures, such as were adopted in Porto Rico, St. Gothard's tunnel, the Westphalian coal mines, and other places where uncinariasis prevailed in its severer forms, it would appear that in the

Philippines hookworm infections play a part more nearly resembling that of the other common intestinal worms to which no definite pathology or severe symptomatology is usually attributed.

In other words, the population of the Philippines presents a higher percentage of infection with intestinal worms than has ever been definitely reported from any other people and the condition is essentially a chronic one, the results of which manifest themselves indirectly in the general physical impoverishment of the people and the high rate of morbidity and mortality accredited to other diseases.

In this connection it is interesting to mention the startling results apparently accomplished by the Bureau of Health, in coöperation with the Bureau of Science, at Bilibid Prison, where the original annual rate of mortality was reduced from about 238 per thousand to about 75 per thousand by the institution of general sanitary measures; then resisted further reduction until the prisoners began to be systematically treated for intestinal worms; after which, the death rate dropped to about 13 per thousand. Whether or not this apparent relationship between intestinal worms and the death rate at Bilibid will be substantiated by future records at the prison or by the institution of a similar campaign throughout the Islands, its significance can scarcely be overestimated even though ultimately the results should prove to be but a fraction of what was apparently accomplished among the Bilibid prisoners, and it sharply emphasizes the fact that the absence of direct, acute manifestations of intestinal helminthiasis should not blind us to the vital importance of this so nearly universal prevalence of intestinal worms as a factor in the present hygienic and industrial status of the Filipino people.

When we consider that there are about 6,000,000 inhabitants in the Islands and that, if present indications are verified, nearly 5,000,000 are infected with intestinal worms, and when we consider further the sanitary conditions which universally exist outside of the larger cities, the magnitude of the problem presents itself, and while we believe thoroughly in the local efficacy of the immediate institution of vigorous crusades by such means as are already at hand, it would seem perfectly apparent that any means which are to reach conditions in the mass of the population must aim at the education and training first of the native physicians and ultimately of the people themselves.

By giving medical zoölogy a prominent position in the course of instruction it is intended properly to emphasize the local importance of the subject which the above indications would seem to warrant, and it is the purpose of the school not only to train its native students in the diagnosis and treatment of parasitic diseases, but also to instruct them thoroughly in the life cycles of the parasites, modes of infection, and methods of prophylaxis, in order that they may be sent out not only as general practitioners realizing the importance of treating infections with intestinal worms, but also to serve as sanitary officers in the towns, municipalities and provinces of the Islands, capable of intelligently enforcing sanitary regulations against animal parasites and of instructing the people concerning the reason and necessity of the measures enforced.

PHILIP E. GARRISON.

OCCURRENCE OF TUBERCULOSIS IN ONE HUNDRED AUTOPSIES IN THE PHILIPPINE ISLANDS.

In a consecutive series of necropsies at the Philippine Medical School, active tuberculosis was found in thirty-four of the first one hundred cases and was with its complications, the cause of death in all but two of the thirty-four.

The lungs were involved in thirty-three cases, the disease in the other being apparently confined to the peritoneum, careful search failing to reveal any tuberculous focus elsewhere in the body. The most frequent type of lesion in the lung was the chronic, ulcerative form of the disease which occurred in twenty-four of the cases. The amount of lung tissue involved in this type of the disease was in many instances remarkable. More or less involvement of all lobes of both lungs, with a minimum amount of air-containing alveoli was present in seven of the series; of both upper lobes in five; of all lobes of the right lung in one; of the entire left lung in two; of all lobes of both lungs except the right middle, in one; of all the left lung and right lower in one; of the left upper in two; of the right upper in one; of the right lower and left lower lobe respectively in one each.

The miliary type of tuberculosis was found in five cases, in two of which it was the only form of lesion present and of the remaining seven, four showed caseous nodules as the prevailing lesion; a gelatinous pneumonia occurred in two and a chronic fibroid in one case. In all of the thirty-three autopsis there were lesions of the pleuræ varying from localized adhesions to complete obliteration of one or both pleural cavities, with varied fibrinous and calcareous changes.

Renal tuberculosis occurred in four of the above cases, the left organ being involved in two, the right in one and both in one. In one instance of kidney involvement the right suprarenal was also tuberculous and in addition one other case of suprarenal tuberculosis was encountered involving both glands, with no involvement of the kidneys.

Twenty of the cases of pulmonary tuberculosis showed caseation of the bronchial glands; three, similar lesions of the mediastinal; five, of the mesenteric and three, of the retroperitoneal lymph glands.

Lesions of the intestinal tract occurred as follows in seven cases: Ulceration of the upper part of the jejenum, one case, one of the ulcers having perforated; of the ileum alone, one; of the colon alone, two cases; of both ileum and colon, two. A general tuberculosis of the peritoneum was found in seven cases, in but one of which was there involvement of the intestinal mucosa.

Of other organs involved, the spleen contained foci in two, the vertebræ in two, and the bladder in two cases.

Against the thirty-four cases of active tuberculosis, healed tuberculous lesions were found in but eight of the one hundred bodies.

PHILIP H. GILMAN.

The Philippine Agricultural Review

A MONTHLY ILLUSTRATED REVIEW PRINTED IN ENGLISH AND SPANISH AND
PUBLISHED BY THE BUREAU OF AGRICULTURE FOR THE
PHILIPPINE ISLANDS.

Edited by G. E. NESOM, Director of Agriculture.

The Philippine Agricultural Review, a newly established publication of the Bureau of Agriculture, will take the place of the press bulletins heretofore issued by that Bureau. It will not be a technical journal, but rather a popular serial publication on general agriculture. The primary object of the *Review* is to furnish an educational means of reaching the people of the Philippine Islands with the work of the Bureau of Agriculture.

The first number of the *Review* is devoted entirely to the annual report of the Bureau of Agriculture for the past fiscal year. This report is so published for the purpose of giving to persons interested in Philippine agriculture a comprehensive idea of the organization, scope, and extent of the work of that Bureau. Succeeding numbers will contain reports on agricultural conditions in different parts of the Philippine Islands, articles on tropical agriculture, and other material of interest to readers of agricultural literature.

Volume I, beginning January, 1908, will be issued monthly, and will be circulated free of charge in the Philippine Islands. A limited number of copies will be sent free to foreign workers along agricultural lines in recognition of valuable services rendered the Bureau of Agriculture. Should there appear to be a demand for regular foreign subscriptions, arrangements will be perfected later for furnishing them at a reasonable price.

Persons receiving the Philippine Agricultural Review are invited to submit material for publication. Any reports, articles, or notes on agricultural subjects will receive careful consideration and, as far as practicable, will be published.

Applicants for the *Review* should state whether the English or the Spanish edition is desired. Address all communications relative to this publication to the DIRECTOR OF THE BUREAU OF AGRICULTURE, MANILA, P. I.

THE PHILIPPINE
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B. MEDICAL SCIENCES

VOL. III APRIL, 1908 No. 2

THE INFLUENCE OF SYMBIOSIS UPON THE PATHOGENICITY OF MICROÖRGANISMS[1] (THE EVOLUTION OF PARASITISM).

By W. E. MUSGRAVE.
(From the Biological Laboratory, Bureau of Science.)

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ANIMAL AND BACTERIAL SYMBIOSIS.
CONCLUSIONS.

INTRODUCTION.

Symbiosis may be defined as representing all phases of association between living organisms, beginning with commensalism on the one hand and including true parasitism on the other, in which either component is influenced in nutrition, metabolism, production, or in some other manner by the presence of the other. Expressed in this broader sense, the subject should be one of interest and its study and the elucidation of its problems one of far-reaching practical importance.

There can be no reasonable doubt but that the symbiotic combinations between microörganisms are responsible for many uninterpreted phenomena in the etiology and pathology of disease, and failure properly to appreciate the existence of these combinations has been one cause of lack of progress in serum therapy. When one studies the rather meager and scattered literature on the subject, notes the promising suggestions that have been given from time to time by great masters, and carefully examines the interesting and often startling results of individual experiments, it is surprising that the subject has not been more minutely investigated. The present paper is general in character, much of it is theoretical, but in important points the conclusions are largely based upon facts.

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[1] The President's Address, read at the Fifth Annual Meeting of the Philippine Islands Medical Association, February 26, 1908.

Nature is filled with examples of diverging biological activities. Frequently living organisms derive benefit by association; and again the presence of one organism or its products may be inimical to the life and growth of certain other forms. These facts are not confined to animals and the higher forms of plant life, but also exist so low down in the scale as to be found among the bacteria. They manifest themselves in many ways; for example, in the study of immunity the symbiosis of microörganisms has an intimate, important and much neglected place. Immunity in any instance is a very specific substance or condition and its specificity and other properties, both known and unknown, may be modified or destroyed in many ways. Among the unknown class, more light needs to be thrown upon the influence which the metabolism of both host and parasite exerts. There is evidence to show that changes in symbiosis may produce changes in metabolism and also, as a result of this, changes in the pathogenic character of parasites and in the susceptibility of hosts.

It certainly seems reasonable to assume that changes in the substances which are the stimulants calling forth the development of immunity *would result in a modification of the type of the immunity itself.* In other words, it is not inconceivable that the immunity unit is a molecule, as it were, the composition of which might be influenced by all agents reacting in its production, and that these agents might be somewhat different, even in the same disease, if they are developed under different environments. Theobald Smith [2] probably had some such idea in mind when, in his classical discussion of the parasitism of the tubercle bacillus, he stated that "In our haste to take the animal and bacterial mechanisms to pieces and to test the individual tissues and components, we have crowed out the broader view that the host fights more as a unit. We had almost forgotten to take into consideration the flexibility and adaptability of the microörganisms themselves."

It is probable that in our study of the manner in which microörganisms produce disease we have not only confined our work too closely to investigating the component parts of the invader and invaded and have not considered the two subjects as a whole, but the weakness probably extends still further and we have failed to consider the environment or symbiosis of both organisms and the influence which this environment or symbiosis may exert upon the metabolism, the toxic and the resisting properties of each, as well as the interaction of the two symbiotic elements which leads to disease or death on the one hand or to what Smith calls a "condition of balanced parasitism" on the other.

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[2] *J. Am. Med. Ass.* (1906), **46**, 1247.

For example, it is well known that certain cases of diphtheria complicated by severe streptococcus infections are not benefited by antitoxin nor are they cured by the administration of both antidiphtheritic and specific antistreptococcic serums. It is probable that one reason for failure in this instance is to be found in the fact that the toxic principle is not a simple mixture of two toxins, but that it has the nature of a new, definite, chemical compound, formed by the symbiosis of the two organisms and therefore producing a type of poison differing not only from that secreted by either, but also from any simple mixture of the two. If this should be true, it would seem altogether probable that the proper immunity unit could only be produced by the action upon animal tissues of the compound toxin radical acting as a whole.

BACTERIAL SYMBIOSIS.

Before taking up a discussion of the influences which symbiosis may exert upon the components produced by any bacterial coexistence, it is necessary to remember that there are many other elements of environment *which may exert an influence on pure species of bacteria,* similar perhaps in results to the manifestations of the same influences on such organisms in symbiosis.

Variability in the virulence of bacteria is one of their most marked features and the reason for this variability is but partially understood. We know that it may be modified by many familiar methods, but no fixed rules can be made or applied. The majority of pathogenic bacteria lose more or less of their virulence by growth upon artificial media and similarly their virulence is increased by passage through susceptible animals. However, this is not always true nor does it explain the variability. For example, there are bacteria which retain their virulence in artificial cultures and others in which this property may be considerably modified by the composition of the medium. Again, it may happen with bacteria that passage through animals will cause a permanent attenuation in some and in others increase of virulence, which for one species of animals may be coëxistent with a weakened virulence for some other species.

A satisfactory explanation of some of the alterations in virulence and of certain of the peculiarities in reactions between bacteria and animal tissues is found in what is now generally known as the hypothesis of Welch which, succinctly put by Ricketts, is as follows: "If bacterial toxins and the constituents of bacterial cells so act on the tissue cells that the latter produce bodies (antibodies) which are inimical to the bacteria, why may not the body fluids in turn so act on the bacteria that the latter produce bodies (antibodies) which are inimical to the tissue cells? Looked at from the point of view of the bacterium, as well as from that of the animal host, according to the hypothesis advanced, the struggle between the bacteria and the body cells in infections may be conceived as an immunizing contest in which each participant is stimulated by its opponent to the production of cytotoxins hostile to the other, and thereby endeavors to make itself immune against its antagonist."

If this hypothesis be true, and it certainly seems to be a reasonable one, the evolution of parasitism, even in pure cultures of bacteria would seem at least in part to depend upon the influence of other agents in supporting, or hindering, the development of either of the elements—parasite or host.

Theobald Smith[3] in discussing the parasitism of the tubercle bacillus, and bearing upon this point, "assumes as a basis for discussion a complex relationship established in time by a selective adaption between two living organisms, of which one is a parasite of the other."

"Whatever pathologic processes of a constant character are the expression of this parasitism * * * are regarded as the result of an interaction of two organisms rather than the work of one alone."

"Viewed from this standpoint, this tendency toward a state of equilibrium between host and parasite is disturbed by any change of condition which influences either parasite or host." Again, the same author believes "that the tendency of infectious disease is toward a balanced parasitism, with a reduced mortality, but not necessarily a reduced morbidity as a result."

This, Theobald Smith considers to be due to a selective action of both host and parasite. In the case of the tubercle bacillus, the very attenuated forms would become, as it were, the parasites of the sick lungs, rather than of the normal ones and would take the same position which pneumococci, streptococci and staphylococci occupy in the upper air passages.

Klein[4] in discussing the question of the evolution of bacteria from saprophytes to parasites concludes that "there is evidence to show that an ordinary saprophyte under altered conditions can produce pathogenic effect, thriving in the tissues of an animal; and that a microbe, under one condition an ordinary saprophyte, can raise itself not only to parasitic life, causing pathogenic action, but further to a parasitic action which is as specific as that of the *Bacillus anthracis* or *Bacillus influenzæ.*"

There are numerous additional facts which tend to support the evolutionary theory of parasitism. For example; under different circumstances the tubercle bacillus may manifest any rôle from the saprophyte to the most exquisite and highly specialized tissue parasite, and there is evidence tending to support the hypothesis that the higher parasitism results from an evolution as it were, produced by many factors, of which symbiosis is one. Most of the primary lesions brought about by the bacillus are formed in or near the skin or mucous surfaces and are probably influenced symbiotically or otherwise by the complex bacterial flora constantly present in these places and by the resulting modified tissue.

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[3] *Ibid.* (1906), 46, 1247.

[4] *Lancet* (1904), 2, 1477.

I may quote a few of the most important observations of others in taking up somewhat more in detail the question of symbiosis between bacteria.

Ludwig Hektoen has stated as follows: "It is conceivable that in some cases the combined action of two microörganisms may be necessary to cause a disease. The nontoxic products of two may synthesize to form a toxic substance."

Richie,[5] in his discussion of the general pathology of infection, remarks that "A study of the correlation and interaction between the various organisms frequently or almost invariably found together, may in the future explain many clinical phenomena and observations as yet obscure." And again the same author writes as follows: "The metabolic *products of certain, it may be harmless, microörganisms are often capable of rendering a nonpathogenic genus pathogenic.*"

It is generally accepted that many of the bacteria normally found in the intestine may under proper surroundings produce disease. Symbiosis is undoubtedly one factor in these changes. Vallagussa found that colon bacilli from the intestines of cats were more virulent when a vegetable rather than a meat diet was given to the animals and that the same bacilli were more virulent when taken from decomposing fæces than when secured directly from the intestine. Coco demonstrated that the virulence of colon bacilli was increased by the presence of streptococci and staphylococci, for mixed cultures caused fever when introduced into the intestines of animals, while pure cultures of either did not do so.

Atlasoff[6] found that *B. typhosus* grew better in acid media in symbiosis with *Torula rosæ* and that when these symbiotic organisms were fed together to young rabbits, a fairly typical typhoid disease was produced.

M. Neisser cultivated on blood agar, colonies of influenza and xerosis bacilli from a case of conjunctivitis caused by measles. He continued the cultivation of the mixed bacteria on ordinary agar, and was successful for twenty generations with an organism which, before his work, had never passed beyond two generations. The influenza bacillus would not grow on ordinary agar without *B. xerosis*. When dead xerosis bacilli were used, the cultures failed and this fact proved that it is not the body of the *B. xerosis* which aids the growth of the other organism, but rather its fermentative action on the medium. Klein[7] showed that bacilli of the Gaertner group had an enhancing value on the virulence of *B. typhosus* when they were grown together with the latter in culture tubes.

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[5] Albutt's System Med. (1907), 2, pt. 1, 1-198.

[6] *Ann. Inst. Pasteur*, 18, 701.

The mechanism by which the facultative aërobic spirillum of cholera, acting in the anaërobic environment of the intestine, produces such intense toxæmia has not been satisfactorily explained and the influence which symbiotic bacteria may exert here needs to be investigated. Several years ago Nägeli advanced the hypothesis that cholera was the result of the coöperative action of two kinds of bacteria. Experimenting along this line Metchnikoff found a bacterium which greatly increasd the pathogenic action of *S. choleræ* and Nencki has described bacteria which in themselves were nonvirulent, but which added greatly to the virulence of *S. choleræ* when they were grown together. Musgrave and Clegg have maintained the virulence of a strain of *S. choleræ* for more than one year by growing it symbiotically with amœbæ. The same strain grown pure on artificial media lost much of its virulence during this time.

There is abundant evidence to show that the symbiosis of the diphtheria bacilli and of the streptococci enhance the virulence of both organisms in many cases of diphtheria complicated by streptococcus infection.

There are also certain bacteria and products of bacteria which are antagonistic to other bacteria or diseases. Emmerich, Low[8] and others have fully established an active antagonism of the products of *B. pyocyaneous* for the anthrax bacillus and for several other organisms. In a somewhat similar manner Rettger[9] and others have proved an antagonistic action of the products of *B. prodigiosus* for certain other bacteria. Turro[10] found that subcutaneous injections of beer yeast would protect rabbits aginst otherwise fatal inoculations of streptococci and staphylococci. This work has also been confirmed and amplified by other observers. Lode[11] cultivated a diplococcus which possessed marked antagonistic properties toward several well-known bacteria, among them staphylococci, *B. anthracis*, *B. cholera susis*, *B. typhosus* and the cholera spirillum. This diplococcus not only had the power of destroying these bacteria in cultures, but this property was also present in Berkefeld filtrates of the cultures.

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[7] *Lancet* (1904), **2,** 477.

[8] Emmerich and Low: *Ztschr. f. Hyg. u. Infectionskrankh.*, Leipz. (1899), **31,** I; *ibid.* (1901), **36,** 9. Emmerich: *Centrbl. f. Bakteriol. Orig.* (1902), **32,** 82. Low and Korschun: *Ibid.* (1902), **31,** 1. Emmerich and Trommsdorff: *Ibid.* (1903), **33,** 627.

[9] *J. Infect. Dis.* (1905), **2,** 562.

[10] *Centrbl. f. Bakteriol. Orig.* (1903), **34,** 22.

[11] *Ibid.* (1903). **33,** 196.

Conradi and Kurpjuweit[12] showed that the growth of *B. typhosus* and *B. paratyphosus* was definitely inhibited by *B. coli*. The inhibiting and antagonistic action of *B. coli* toward some other organisms has been shown by a number of authors.

Gabricewski and Maljatai[13] found that *S. choleræ* inhibited the growth of *B. coli*.

Heineman[14] found that streptococci isolated from milk interfered with the development of *B. lactis aërogenes*.

Herter[15] has demonstrated repeatedly that streptococci grown from the human intestine may repress cultures of *B. coli* from the same source.

Walker showed that the typhoid bacillus when grown in the presence of its antiserum acquires a greater virulence for animals and that a larger dose of protective serum is necessary to save guinea pigs from infection with the immunized culture than is needed to protect from the same strain which had not been immunized. Wechsberg demonstrated that diphtheria bacilli could be made to produce a larger amount of toxin by adding diphtheria antitoxin to the culture media in which they are grown.

Many more examples of the above conditions might be mentioned, but these suffice to show the influence which surroundings, even in the test tube, may have upon cultures of bacteria. This influence might properly be considered under the headings of *nutrition, metabolism* and *production,* and the relation between these three conditions is surely more close and significant than we are accustomed to consider it to be in laboratory technique. If such influences as these may modify our artificial cultures of bacteria, how much greater may be the effect upon the three factors mentioned above of the more complex conditions surrounding mixed cultures in unknown symbiosis. Furthermore, what a mass of additional factors are brought forward when we attempt to study the results of the three we have considered, acting and reacting between such a complex of organisms and the animal tissues.

Vaughan, in studying the chemistry of bacterial cells, found that so many definite bodies could be split off along fixed lines of cleavage that he concluded the bacterial cell to be made up of a compound of various chemical groups. If this hypothesis be true it seems reasonable to believe that the character of the various chemical groups would depend partially, at least, upon the character of the substances which may be brought together in the environment.

Ricketts, in discussing the hypothesis of Welch, says: "Certain constituents of our body fluids may, by combining with suitable bacterial receptors, stimulate the bacteria to the production of a whole shower of cytotoxins * * * the nature of the animal substances * * * is not of essential importance * * *. It is not necessary that they be toxic for the bacterium and they may even be taken up as food substances."

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[12] *München. med. Wchnsch.* (1905), **52**, 2164, 2228.

[13] *Centrbl. f. Bakteriol.* (1893), **13**, 780.

[14] *J. Infect. Dis.* (1906), **3**, 173.

[15] Bacterial Infections of the Digestive Tract. Macmillan, 1907.

This quotation, again, at least in part, discusses a condition of production, metabolism and nutrition. The requirements of a certain form of production calls for an alteration in metabolism, which in turn may demand a modification in nutrition. The ability to answer the call for production, and therefore a determination of the progress of pathologic lesions, must depend to a certain extent on the ability of the symbiosis to supply the required nutrition.

ANIMAL AND BACTERIAL SYMBIOSIS.

Nutrition, metabolism and production in animal parasites certainly are more complicated than with bacteria, and unless we bear this fact constantly in mind the whole subject of parasitism is apt to be considered along too narrow lines and our specificities to be regarded as too exacting.

The question, just as with bacteria, not only involves a study of the interaction between an animal host and animal parasite, but a study of host under constantly varying conditions being acted upon by parasites influenced by an ever-changing environment.

A battle, as it were, takes place between two sets of very complex influences, leading to death or disease of the host on the one hand, to destruction or commensalism on the part of the parasite on the other, or finally quite frequently to what Theobald Smith has called a condition of balanced parasitism.

Very little has been done bearing directly upon the subject of this interesting question of the influence of symbiosis upon animal parasites and most of the literature available concerns itself with amœbæ. The association of certain animal parasites and bacteria in both saprophytic existence and in pathologic lesions was formerly generally considered to be an accidental one, but the idea that the relations between these various types and combinations are of a definite nature and that such associations exercised a specific influence upon the nature and production of disease processes is of comparatively recent origin, so that the amount of evidence is still distressingly small.

When we closely consider this question we find support for the positive side in the suggestions of many careful observers and in all experimental work with amœbæ. Baumgarten (1890) suggested the probable coöperation between amœbæ and bacteria in the production of dysentery. Janowski (1897) considered it not improbable that the symbiotic organisms may determine the pathogenicity of the amœbæ themselves, and that the symbiosis found in nature may be carried unbroken into the intestine, or that it may be formed in the bowel. Such observations have now been repeated and amplified by so many authors that they have appeared in some of the modern literature as proved facts.

Since 1904 Musgrave and Clegg have been publishing the results of researches bearing directly upon this subject. It was first brought forcibly to our attention in the cultivation of amœbæ, which we could not accomplish in a satisfactory manner except in the presence of other living microörganisms, nor has a larger experience and maintained interest given any different results. From the first, the association of bacteria and amœbæ appeared to be very intimate and subsequent work which has been published and need not be reviewed here, has demonstrated some such association to be necessary for the propagation of amœbæ under any circumstances but those of pure parasitism. As a result of more than four years of this continuous work the following suggestions are offered:

1. Amœbæ in any natural environment, whether outside or within the body (excepting in certain liver abscesses and a few other situations), lead a parasitic life in that they feed upon, or in some other way sustain life by the presence and often if not usually at the expense of other living microörganisms.

2. This symbiosis, even when the parasites are in a very mixed bacterial environment, is more or less specific for certain elements of this environment.

3. This specific character of the symbiosis may be changed in artificial media and the evidence points to the occurrence of such changes in nature.

4. All the parasites present in any given environment—the intestine included—are not in symbiosis with the same bacterium.

5. If amœbæ in symbiosis with a given bacterium, after introduction into the intestines of animals, succeed in remaining and propagating there, it is usually by a change of symbiosis to an organism which was already present in the intestine.

6. All amœbæ which reach the intestines of animals in a viable condition, whether as spores or as encysted or vegetative parasites, probably do so either in an active symbiosis, or in a receptive condition for some more or less special symbiosis. The question of proliferation in the intestine probably depends—at least at first—upon the maintenance for a time of the old symbiosis or the ability to change to another one with living microörganisms present in the bowel.

7. During this primary stage of intestinal infection and so long as the true bacterial symbiosis in maintained, it is probable that no particular harm is done to the bowel, regardless of the source or variety of amœbæ present. However, as soon as the tissue components or secretions begin to influence the metabolism or effect other changes in this bacterial-amœbic compound, it is not unreasonable to believe that return manifestation toward the tissues may become a property of the amœbic-bacterial symbiosis, and that lesions of the bowel result.

8. From this amœbic-bacterial-intestinal compound lesion some process may be evolved changing the metabolism of the parasite and lowering the tissue resistance until a focus of infection in which the bacteria have been eliminated, is established in the liver, brain, spleen or some other organ, and thus a lesion is produced which is due to an interaction between the amœba and the animal tissues, a condition of true animal tissue-parasitism.

9. In considering the occurrence of true parasitism we must never lose sight of the fact that the amœba is altered as well as the tissue, which by change has become capable of being the host of the microörganism.

Among the higher animal tissue-parasites in which bacteria play no part in the symbiosis, we still have modifications due to environment, just as are shown by pure cultures of bacteria.

Lingard,[16] showed that the virulence of *Trypanosoma evansi* is to a certain extent influenced by conditions which affect the pathogenicity of bacteria. This author passed an organism of surra directly from horse to horse through forty animals. During the first part of the experiment the incubation period varied from four and one-half to six and one-fourth days and the duration of illness from twenty-five to forty-two days, but during the latter period the incubation time was reduced to from three to four and one-half days, and the duration of the disease to from three to four days. The author made the further interesting observation that white mice inoculated from a horse in the early stage of his experiments showed an incubation period of from five to five and one-half days and a duration of the disease of five days. The infection was then transferred from mouse to mouse, and between the thirty-seventh to forty-seventh mouse instances occurred in which the incubation was reduced to twelve hours and the course of the disease to from two and one-half to three days. Still more interesting is the fact that a horse inoculated from the forty-seventh mouse lived four and one-half times as long as the control animal.

Some of the influences which a change of host may exert on parasites are well illustrated in smallpox. As is known, the pustular contents of smallpox when inoculated into monkeys produces a disease which clinically may closely resemble variola in man. When some other of the lower animals, such as the cow, are used for these experiments, the disease reproduced in the animal differs materially in its manifestations and when the virus is again transferred from the cow to man it manifests itself as vaccinia, which differs from smallpox, and human variola can not be reproduced from this virus.

Satisfactory explanation of this phenomenon has not been furnished beyond the obvious fact that in some manner the pathogenic character of the organism is changed. Great variations in the pathogenic nature of the cause of smallpox, which are due to other influences, are shown in the marked difference in the severity of the disease in various epidemics. Not infrequently the disease in certain outbreaks may appear to be so mild as fairly to justify the statement that the infection is harmless, and again under apparently similar conditions or during the same epidemic, the reverse condition of severe infection and high mortality may obtain. Such changes are probably not due to a difference in the condition of the host as is the case in vaccinia, but to some other symbiotic or environmental influence acting with or upon the parasite, and as Professor Councilman has pointed out, the part played by the constantly present symbiotic bacteria in these lesions has not yet been determined, but it is probably an important one.

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[16] Annual Report, Imp. Bact. of India (1906–7).

CONCLUSIONS.

It seems to me that the evidence is fairly conclusive in favor of a more or less definite symbiosis, for example between amœbæ and other microörganisms, whether they be found in a saprophytic existence or in pathologic lesions, with the exception of the true animal parasitism found in certain bacteria-free abscesses in the animal host, and this parasitism is evolutionary in character.

In other words, a condition of parasitism exists even under outside conditions, a parasitism between bacteria and amœbæ which is not only a changeable one, but which may be evolutionary, gradually passing from the extraneous surroundings to be found in water and other saphrophytic environment, through the mixed infections encountered for example in dysenteric ulcers, where the elements of nutrition of the amœbæ may consist of animal secretions or tissues, modified or reënforced by the bacteria, to a condition of true animal tissue-parasitism found in certain abscesses of the liver and other places in the body, or even to the still more exquisite parasitism of amœbæmia, two cases of which have been observed by Mr. Clegg and myself.

There does not appear to be anything particuluarly radical in such a hypothesis, especially when one considers what has been proved about the action of mixed cultures of bacteria in respect to symbiosis and when it is remembered that at least that part of this evolution of parasitism in which amœbæ pass from the mixed environment of the intestinal lesion to a more specific tissue parasitism is a matter of routine observation in the tropics.

I am convinced, as has been stated above, that such an evolution of parasitism from an amœbic and bacterial symbiosis in water or elsewhere in nature, through a beginning or mixed tissue and bacterial parasitism in amœbic ulcers of the colon, to a true tissue parasitism in the internal organs of the body, or even to a blood invasion itself, is a matter of frequent occurrence. However, the extent or generality of such a process and the elements necessary for its beginning and propagation and the influences which antagonize or favor it are only slightly studied.

The whole question is of the most intense interest and of the greatest practical importance and offers one of the most promising fields for research to be found at the present time. It is not inconceivable that the whole process of parasitism, even in its greatest selectiveness, as for example of tetanus toxin for the nervous system or of certain trypanosomata for cerebro-spinal fluid, is evolutionary and there is not lacking evidence which may be used in support of such a hypothesis with more logic than has hitherto been given in attempted explanation of many phenomena.

The most promising field for laboratory research in the future will be the study of cause and effect, in the complex relations in which they occur in nature, of the interrelation and interaction of microörganisms with each other and in their environment of complex symbiosis and the ever-changing and multiple conditions found in hosts. Attention to individual components of microörganisms and specific manifestation of resistance by hosts without being accompanied by a balanced conception of the influence of complex environment upon the details, has undoubtedly led to the elaboration of a considerable superstructure which is useless if not dangerous in the study of pathology.

SOME CONSIDERATIONS WITH REGARD TO THE CAUSE OF THE FREQUENT REAPPEARANCE OF CHOLERA IN THE PHILIPPINE ISLANDS, WITH STATISTICS BEGINNING WITH THE OUTBREAK IN 1902 TO JANUARY 1, 1908.[1]

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INTRODUCTION.

The Bureau of Health has been called upon to combat cholera more or less continuously from the time of the publication of the paper which was read upon the subject of cholera before the Manila Medical Society January, 1906,[2] up to the present. The total number of cases and deaths reported from the beginning of the outbreak in 1902 to January 1, 1908, was as follows:

TABLE I.—*Cases and deaths from cholera in the Philippine Islands from the beginning of the outbreak in 1902 to January 1, 1908.*

Date.	Cases.	Deaths.
March 2, 1902, to March 8, 1904	166,252	109,461
March 8, 1904, to January 1, 1908	11,691	8,654
Total	177,943	118,115

Mortality, 74.03 per cent.

It is apparent from the foregoing figures that cholera has caused great havoc in these Islands. This is greatly to be deplored not only from the standpoint of the useless loss of human life, but also because such conditions retard the development of the country by reducing the already too small number of workers.

At first sight it would appear as if the diffusion among the masses of the plain, simple truth, that cholera can only be contracted by the introduction into the mouth of contaminated food or drink, and that almost absolute safety against infection can be insured by the simple precaution of using sterilized water and cooked food, would result in its early disappearance, but when it is remembered that the climate is favorable for the development of the cholera organism throughout the four seasons of the year—in other words, that there is no winter season which would at least stop the disease for a time—that a large portion of the people are ignorant and inaccessible, that much superstition exists, that one of the most popular beliefs is in the supposed injurious character of boiled water, that the cost of fuel is comparatively high, making sterile water and cooked food difficult for the masses to obtain, that the majority of the people cling tenaciously to the mode of living which has been customary with them for hundreds of years, that food is conveyed to the mouth with the fingers from a receptacle used by all the household, that over 60 per cent of the population are afflicted with intestinal parasites, that, with the possible exception of the supply for a few hundred thousand out of a total of seven million, the drinking water is obtained from shallow surface wells, that physically the people are weak and unresistant, and that funds and skilled physicians needed to combat this condition are very limited, it will not be so difficult to understand the continued presence of cholera in the Philippines. If better results or the complete eradication of the diseases are to be hoped for, additional methods beyond those which have heretofore been used in any part of the world will need to be made available. In order that such methods may be determined upon in a scientific manner, it will be necessary to make further advances in the study of the cholera organism, both from a morphological and epidemiological standpoint. The following deductions based upon observations of the cholera during the past five years are submitted with the hope that some progress may be made in this direction.

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[1] Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, February 28, 1908.

[2] *J. Am. Med. Ass.* (1907), 48, 856.

PAST EPIDEMICS IN THE PHILIPPINE ISLANDS.

It will perhaps be recalled that the first case of cholera, recognized as such since American occupation, occurred in March, 1902. It is difficult to determine satisfactorily whether any cases of the disease had occurred between the epidemic of 1888 and of March, 1902. This is a question, however, which has given rise to considerable discussion. Physicians who were resident in the Philippine Islands prior to American occupation claim that cholera has been continually present for many years, but it is generally held by Americans that because no record exists of a microscopic confirmation of such cases, the diagnoses are open to doubt. In view of the foregoing, it is of course evident that this question can never be definitely and satisfactorily settled. Certain it is, however, that between 1897 and 1902 there is no record of any other disease in the Philippine Islands which shows such a large mortality, nor was any such infection present in so many portions of the Islands as has been the case since 1902. The commencement of the disease in 1902 was ascribed to a shipment of presumably infected Canton cabbage arriving in Manila from Hongkong which upon being refused landing, was thrown overboard in the harbor, with the result that the whole bay was literally covered with this vegetable. Much of the cabbage was gathered and consumed and within forty-eight hours from the time of its reaching the beach, cases of cholera commenced to occur in the Farola district[3] (see Pls. I and II), which is situated at the junction of the Pasig River and Manila Bay. An Army transport which left Manila at about the same time these vegetables were thrown overboard, proceeded directly to Nueva Caceres and the disease was discovered among some steerage passengers of this ship after they had landed, so that cholera appeared simultaneously in two widely separated places in the Philippine Islands.

The infection spread rapidly in Manila in spite of the most energetic measures which were taken to combat it. The cordon which was placed around the city was entirely ineffective and apparently offered little resistance to the onward march of cholera. Infected persons gradually introduced the disease into the other islands. The outgoing maritime quarantine imposed upon vessels was ineffective because people traveled overland to ports at which there was no adequate quarantine inspection, and sailed from there. Cholera raged with great severity for nearly six months in and about Manila (over 6,000 cases occurring in this city alone) and it continued for about an equal length of time in other portions of the Islands, after the date of its first appearance. There was a rather severe recrudescence during the following year in Iloilo and Cebu. The Board of Health for the Philippine Islands on April 27, 1904, officially declared the disease to have been completely arrested, and stated that no cholera was then in the Islands.

The next appearance in recognizable form took place in August, 1905, when persons in the neighborhood of Jala Jala, in the Province of Rizal, on Laguna de Bay (see Map No. 1), commenced to die from the disease, and from there it apparently spread rapidly down the Pasig River to Manila. Since 1905 the disease has been practically confined to Manila and the provinces which are accessible by land from this city. The only exceptions to this rule are the outbreaks which occurred in the Provinces of Iloilo, Occidental Negros, northern Samar, Mindanao, and Leyte.

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[3] The Farola district is a narrow neck of land running out into the sea and having the main harbor light at its point. It was occupied at the time of the outbreak of this epidemic by warehouses, coal piles and a crowded mass of small, insanitary huts.

CHOLERA-LIKE CASES PRECEDING TRUE OUTBREAKS.

It is noteworthy that between March, 1904, and August, 1905, cases resembling cholera were encountered every few weeks in and about Manila. These died with practically all the clinical symptoms of cholera, but upon bacteriological examination, cholera vibrios could not be demonstrated in the stools or at autopsy. This fact has received considerable attention and since 1905 it can definitely be stated that the last three outbreaks in Manila, namely that of August, 1905; of June, 1906, and of August, 1907, were invariably preceded by suspicious deaths of the kind mentioned above. Cases suspicious of cholera occurred at intervals of one to four weeks in various sections of the city of Manila as early as April, 1905.[4] Possibly, in all, from 10 to 15 deaths of this kind in which a positive microscopical diagnosis could not be made came under observation before each outbreak. In view of the fact that all deaths in the city of Manila are investigated before a burial permit is issued, it is not likely that many of these cases escaped observation.

Even after the disease establishes itself it rarely happens that two infections occur in any one house or in a group of houses, or even in the same block. The isolation of the case and the prompt disinfection which is made of the premises in each case may account for this fact in part.

OTHER OBSERVATIONS IN REGARD TO THE EPIDEMIOLOGY.

Many isolated observations, which seemed in some way to be intimately connected with the spread of the disease were made since 1903. It has been noted that when flies are particularly active and persistent and refuse to be driven away, as, for instance, is the case in the United States before a thunderstorm, or when large numbers of roaches, water bugs, and other vermin were seen to be moving about actively in the streets, or when the humidity is relatively high, or bright sunshine is absent with only a small amount of rain, immediately a considerable increase in the number of cholera cases almost invariably follows. In 1903 it was observed that the still water in the bends of the Pasig River was infected with cholera organisms, while the main current of the river remained uncontaminated.

The outbreak of the disease, for instance in Manila, practically always commences among the lowest members of society and frequently beggars or other persons who eke out a precarious existence are the first to be attacked. An examination of the order in which cases appeared in the city of Manila during 1905 and a comparison with the subsequent outbreaks shows that the same condition of affairs which existed then has been present ever since, namely, one case will occur in Tondo district, the next possibly in Malate, the next perhaps in Sampaloc, all generally a mile or more apart, and the most careful investigation fails to reveal any connection whatsoever between the infections. After this beginning the disease seems to increase in virulence and gradually commences to attack persons who are better nourished and fed, until finally more resistant persons like Europeans, the better class of Filipinos, and Americans become victims.

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[4] *Loc. cit.*

It has been most difficult to explain the presence of cholera in Bilibid Prison each time that it makes its reappearance in the city of Manila. In this institution sterilized water is supposed to be invariably furnished and only cooked foods are served and every reasonable precaution is taken. The outbreaks in this institution have heretofore never been satisfactorily traced or accounted for.

The practical observation made several years ago that an outbreak of cholera is never severe in a community which was afflicted within two years has been of great assistance in combating this disease. Another noteworthy fact is that a much larger percentage of cases occurs among the Japanese than among any other nationality, and this is particularly true of the Japanese fishermen who leave the shore every evening at sundown and spend the night upon the bay in fishing; returning again about daylight. These men are usually attacked during the latter portion of the night.

The appearance of the disease in the provinces which are accessible from Manila by land apparently is never preceded by the suspicious deaths which have been observed in this city, and so far there has been very little difficulty in tracing such outbreaks to a previous case. On the other hand, those which have occurred in the Provinces of Iloilo, Samar, and Leyte (see Map No. 2), which are separated from Manila by the open sea, have invariably begun among the poorest members of the community and the first cases could not be traced to a previously infected person.

FACTORS SUGGESTING HYPOTHESIS.

During the past five years in order that improved methods for stamping out cholera might be devised, every endeavor has been made to formulate a hypothesis which would explain the appearance of this disease under such unusual circumstances, but up to within a few weeks ago this has been impossible. In consequence, it has not been practicable completely to eradicate the cholera from the Islands by employing the usual sanitary measures. Of course, it is well known that if all the residents of a community could be induced to drink sterile water and eat cooked foods the disappearance of cholera invariably wuld take place, but with a population like that of the Philippine Islands, it will be obvious to those who have had experience with local conditions that many years of education would be required before a result of this kind could be hoped for; so that if greater success is to be expected, a more direct method of attacking the problem will have to be devised. The fact that the disease seems to reappear in the city of Manila in a form which clinically resembles cholera, apparently offers a key to the problem, especially as it is coupled with the other fact that the study of the organism at the Biological Laboratory of the Bureau of Science by different workers shows that considerable change in its morphology takes place. Clinically, such cases give a history of sudden onset with vomiting which lasts for a period of six to twenty hours, marked diarrhœa with stools not typical of cholera, extreme collapse, severe cramps in the arms and legs, profuse sweats, subnormal temperature, rapid pulse, anuria, and other evidences of intense intoxication, for which active stimulation, external heat, hypodermoclysis, intravenous transfusion of salt solution, or serum are of no avail. On post-mortem these cases show marked rigor; dryness of the abdominal cavity; intestinal contents not typical of cholera; the ileum and large intestine studded with small, bead-like elevations; evidences of intense acute nephritis and punctiform hemorrhages upon the serous surfaces of the heart, and cultures made by such competent observers as the chief of the Biological Laboratory and his assistants fail to reveal cholera organisms. However, each succeeding case gradually approaches more and more the findings of cholera both clinically and at autopsy, until finally the autopsies are typical and the cholera organism is recovered from cultures taken from the intestines. When this stage is reached, the disease also spreads much more rapidly throughout the city, the number sometimes reaching as high as 70 cases per week, with a mortality of 90 per cent; this then gradually declines, and the mortality drops to 40 or 50 per cent. An outbreak of this kind extends over a period of from two to three months. After the organisms once become recognizable, there is no difficulty in identifying them until the disease completely disappears, although there is considerable change in their morphology, which will be shown in a subsequent paper by H. T. Marshall.

The fact that the cause of the outbreak of cholera in the provinces of the Philippines seems invariably to be traced to Manila, the disease either being transmitted by the infected persons or foods, and since the first cases in Manila after 1904 are not traceable to any outside source, it is evident that some conditions must exist in this city favorable to the continuance of the cholera organism which do not obtain in other portions of the Islands. It does not appear probable that the organism remains in a quiescent stage in the intestines of the residents, because in that event there certainly would be many outbreaks in other portions of the Islands of the same heretofore inexplainable kind as these which have occurred in Manila. It seems certain, to judge from our knowledge of the cholera organism, that it could not exist in a dry state and since a constant wet medium is indispensable, it appears probable that the old sewer system of the city of Manila offers one of the few conditions in which the latter is assured during every day in the year. It is scarcely conceivable that a pathologic cholera vibrio is propagated in the city water supply because a much larger number of cases would surely occur.

HYPOTHESIS.

With the conditions then as set forth in the foregoing pages, the following hypothesis is submitted: The cholera organism is continuously present in some form in the sewer system of Manila either in its fluid contents or in vermin; at certain stages of its atypical form, by passage through the human intestine or otherwise, it first is capable of producing a disease resembling cholera, but the organism can not be recognized by the present laboratory methods. Successive passages through the human intestine produce a typical cholera vibrio. Possibly the disease disappears because the population gradually becomes immune by eating fish and other sea products which have been taken from cholera-infected waters, or drinking the water itself. An immunity of this kind appears probable from the fact that cholera organisms continuously passed through the living, susceptible intestines either increase or retain their virulence, and this should cause the mortality among those attacked throughout an epidemic to remain the same. However, the reverse is the case, as may be seen by referring to the history of the cholera outbreaks in the Philippines and other countries (the rate at the beginning being from 90 to 100 per cent and soon falling to 40 per cent or below), so that the decline in the mortality would seem to be due rather to the acquired resistance of the individual than to the change in the cholera vibrio.

CONDITIONS CONFIRMING THE HYPOTHESIS.

It appears probable that the cholera organism is conveyed either directly or indirectly from the sewers to easily contaminated articles of food or drink by the means of roaches, either through direct mechanical contact with their feet or bodies, or by the deposition of their excretions, thence it is passed to human beings; but flies, water bugs, and other vermin commonly found in sewers are also no doubt partly responsible.

When it is remembered that cholera organisms can live in the intestines of such vermin for a number of weeks, it will be at once apparent that many cases of cholera, the origin of which has heretofore been obscure, will have at least a reasonable explanation. It has frequently happened that only one case occurred in a house in which seventy-five persons or more obtained their meals and the fact that rarely ever more than one case occurs in a city block shows a limited infection which can be explained by insect transmission. An outbreak of cholera such as occurred in Honolulu during the latter part of December, 1907, might also be explained by the landing of infected roaches.

As soon as proper health measures are put into effect to provide for the disinfection of the stools of infected persons and the community gradually acquires a temporary immunity, the outbreak slowly subsides, and the disease does not again make its appearance in Manila until it is either introduced from the outside or the cycle given above is repeated.

It is conceivable that the immunity which has been referred to is due to drinking city water, which at times contains a vibrio similar to that of cholera but this does not appear probable. The outbreaks in the provinces which are separated from Manila by open sea seem to be caused by infected food, and this seems especially true if we consider the observation made by Dr. Cullen that the first persons attacked last yaer in northern Samar all had eaten a poor quality of dried fish taken from waters in Manila that were presumably infected.

The fishing industry in and about Manila is conducted on a most extensive scale. The low, marshy character of the section of the bay north of the Pasig River and the rise and fall of the tide, produce ideal conditions for the growth and contamination of shell and other fish, and this is especially accentuated since the tidal currents are such that the contents of one of the city's largest sewers is extensively distributed throughout this area. Granting, then, for the sake of argument, that fish, shellfish, and other sea products become infected with cholera and that through imperfect cooking the organisms are not all killed, and that one of the principal food substances of the masses in the city of Manila is gathered from the section just mentioned, it is evident that it would be possible to immunize a large portion of the city's inhabitants. Enormous quantities of sea products in a dry or partially dry state are also sent to various portions of the Islands from Manila and if it should happen that some of them have been shipped in a moist condition or are otherwise rendered a good culture medium of cholera vibrio, it is conceivable that such products might, in isolated instances, be the cause of appearances of cholera in places such as Samar, Leyte, etc. In view of the fact that this class of food products is the sustenance of the masses because of its cheapness, it is more probable that the underfed members of a community would be the first to be affected by the slight infection which it might contain.

In order to test the foregoing hypothesis, the Bureau of Science has undertaken a laboratory study of the matter, and already investigations made within the past few weeks of the sewers of the city of Manila show that the cholera organism was present in them, and that almost simultaneously with the disappearance of the disease in human beings, about two weeks ago, it has been impossible to find any cholera vibrios in these sewers. In view of the results of this study, it appears probable that the cholera vibrio may live in the old Spanish sewers of the city of Manila indefinitely. This fact may not be capable of demonstration the year around, but the failure to find the organism is due to the change in its morphology. It also appears probable that at such times as the organism can not be recognized as the cholera vibrio, there is a stage during which it is capable of producing cases resembling cholera, such as have been noted in each instance before an actual outbreak.

CONCLUSION.

In conclusion, then, it may be justifiable to state that, it appears highly probable, cholera is endemic in the city of Manila; that the habitat of the organism is in the sewers of the city; that outbreaks in the Philippines outside of Manila are probably due to direct infection from the city of Manila by the food products which are sent out from here, or by direct infection by the means of persons carrying the disease. The cases which occurred in the provinces which can be reached by land outside of Manila are in nearly every instance caused by direct infection by means of human beings, and not from food products. This peculiarity is probably due to the fact that very little food is sent from Manila to near-by towns, because they have similar supplies within their own borders.

Briefly, then, it is believed that if the sewer system of Manila could be throughly disinfected and rendered free of the cholera organism in any of its forms, and the egress of vermin could be stopped, one of the principal sources of the disease would be removed and the early disappearance of the infection from the Islands could be hoped for.

The following tables demonstrate that the average duration of cholera in a town is about two months.

TABLE IV.—*Cholera statistics arranged in the order in which the towns became infected.*

JANUARY TO JULY, 1906.

Date of first case.	Town.	Province.	Highest number of cases.	Date of last case.	Total number of cases.
Jan. 3	**Naic**	Cavite	Jan. 24	Feb. 26	195
Jan. 3	**Macabebe**	Pampanga	May 21	June 28	97
Jan. 4	**Abucay**	Bataan	Jan. 16	Mar. 8	66
Jan. 4	**Bulacan**	Bulacan	Feb. 15	Mar. 2	19
Jan. 4	**Noveleta**	Cavite	Jan. 31	Feb. 3	58
Jan. 4	**Calumpit**	Bulacan	Jan. 15	June 29	65
Jan. 4	**Malolos**	do	Jan. 4	June 30	41
Jan. 4	**Quingua**	do	Jan. 11	June 30	88
Jan. 4	**Imus**	Cavite	Mar. 24	Apr. 5	36
Jan. 5	**Hagonoy**	Bulacan	Jan. 5	Mar. 8	33
Jan. 5	**Lilio**	La Laguna	Jan. 5	Jan. 5	2
Jan. 5	**Magdalena**	do	Jan. 5	Jan. 15	3
Jan. 5	**Majayjay**	do	Jan. 5	Jan. 15	2
Jan. 5	**Paete**	do	Jan. 12	Mar. 7	36
Jan. 5	**Guagua**	Pampanga	Jan. 17	Feb. 5	50
Jan. 5	**San Luis**	do	June 16	June 30	120

TABLE IV.—*Cholera statistics arranged in the order in which the towns became infected*—Continued.

JANUARY TO JULY, 1906—Continued.

Date of first case.	Town.	Province.	Highest number of cases.	Date of last case.	Total number of cases.
Jan. 5	Malabon	Rizal	Jan. 24	Feb. 1	27
Jan. 6	Tarlac	Tarlac	Jan. 30	Feb. 1	8
Jan. 8	San Roque	Cavite	Jan. 8	Jan. 8	1
Jan. 8	Santa Cruz	La Laguna	Jan. 12	June 30	15
Jan. 10	Balanga	Bataan	Apr. 12	Apr. 19	88
Jan. 11	Paombong	Bulacan	Jan. 11	Feb. 26	48
Jan. 11	Cabanatuan	Nueva Ecija	Jan. 11	Feb. 23	42
Jan. 12	Pila	La Laguna	Mar. 7	Mar. 7	2
Jan. 12	Baliuag	Bulacan	Jan. 31	Apr. 18	70
Jan. 12	Lubao	Pampanga	Jan. 25	May 24	56
Jan. 13	San Francisco de Malabon	Cavite	Feb. 2	Feb. 23	57
Jan. 13	Cavite	do	Jan. 26	June 30	20
Jan. 15	Nagcarlang	La Laguna	Jan. 15	Jan. 15	1
Jan. 16	Orion	Bataan	Feb. 21	Apr. 19	84
Jan. 16	Pagsanjan	La Laguna	Jan. 22	June 30	10
Jan. 16	Arayat	Pampanga	Apr. 26	Apr. 28	108
Jan. 16	San Fernando	do	Jan. 19	Mar. 31	5
Jan. 17	Bongabong	Nueva Ecija	Jan. 17	Jan. 17	1
Jan. 18	Stotsenberg	Pampanga	June 13	June 13	2
Jan. 19	Candaba	do	Feb. 5	Mar. 10	49
Jan. 22	Angat	Bulacan	Jan. 27	Mar. 2	127
Jan. 22	Biñang	La Laguna	Jan. 22	Jan. 22	1
Jan. 22	Gapang	Nueva Ecija	Jan. 22	Feb. 20	36
Jan. 22	Apalit	Pampanga	Jan. 22	Feb. 27	59
Jan. 22	Calamba	La Laguna	Jan. 22	June 30	3
Jan. 25	Santa Maria	Bulacan	Jan. 27	Mar. 7	39
Jan. 25	Florida	Pampanga	Jan. 25	Jan. 25	1
Jan. 25	Mexico	do	Jan. 25	Mar. 20	2
Jan. 25	Santa Rita	do	Jan. 25	Feb. 26	8
Jan. 26	San Pedro Macati	Rizal	Jan. 26	June 28	3
Jan. 29	Maragondon	Cavite	Feb. 23	Mar. 10	70
Jan. 29	Angeles	Pampanga	Jan. 29	Jan. 29	1
Jan. 29	Bacolor	do	Feb. 20	Feb. 21	4
Jan. 30	Bocaue	Bulacan	Jan. 31	Feb. 20	14
Jan. 30	Indang	Cavite	Feb. 1	Feb. 13	24
Jan. 30	Peñaranda	Nueva Ecija	Jan. 30	Mar. 27	8
Jan. 30	Porac	Pampanga	Jan. 30	Jan. 30	1
Jan. 30	La Paz	Tarlac	Feb. 6	Feb. 10	10
Jan. 31	Orani	Bataan	Feb. 8	Mar. 16	35
Jan. 31	San Antonio	Nueva Ecija	Feb. 13	Mar. 26	7
Feb. 1	Pangil	La Laguna	Feb. 17	Feb. 17	4
Feb. 5	San Isidro	Nueva Ecija	Feb. 16	Feb. 26	8
Feb. 15	Bagac	Bataan	Feb. 15	Feb. 15	1
Feb. 15	Polo	Bulacan	Feb. 15	Feb. 16	3
Feb. 21	Guevara	Tarlac	Feb. 21	Feb. 26	9
Mar. 5	Siniloan	La Laguna	Mar. 5	June 27	142
Mar. 15	Bacoor	Cavite	Apr. 26	May 21	16
Mar. 19	Capas	Tarlac	Mar. 19	Mar. 19	1
Mar. 22	Mabitac	La Laguna	Mar. 22	Mar. 31	2
Apr. 16	Parañaque	Rizal	May 1	May 23	25

TABLE IV.—*Cholera statistics arranged in the order in which the towns became infected*—Continued.

JANUARY TO JULY, 1906—Continued.

Date of first case.	Town.	Province.	Highest number of cases.	Date of last case.	Total number of cases.
May 1	Pasay	Rizal	June 9	June 30	4
May 29	Mariveles	Bataan	May 29	May 29	1
June 9	Pasig	Rizal	June 20	June 30	61
June 12	Antipolo	do	June 12	June 12	1
June 18	Tanay	do	June 23	June 30	145
June 20	San Felipe Neri	do	June 20	June 30	5
June 22	Nampaya	La Laguna	June 22	June 22	2
June 25	Cabuyao	do	June 25	June 29	2
June 26	Taytay	Rizal	June 26	June 28	10
June 28	Taguig	do	June 28	June 28	1
June 29	Bay	La Laguna	June 29	June 29	1
June 30	McKinley	Rizal	June 30	June 30	1

FISCAL YEAR 1906-1907.

1906.			1906.	1906.	
July 2	Pasig	Rizal	July 7	Sept. 9	108
July 2	Fort McKinley	do		Aug. 16	6
July 2	Pasay	do	July 7	Aug. 17	44
July 2	Tanay	do	July 29	Aug. 17	72
July 2	San Felipe	do		July 20	20
July 2	Lumbang	Laguna		July 2	1
July 2	Santa Cruz	La Laguna	July 15	Oct. 31	132
July 2	Pagsanhan	do	July 15	Oct. 22	11
July 2	Pila	do	July 4	Aug. 30	49
July 2	Malolos	Bulacan	July 30	Aug. 22	145
July 2	Quingua	do			117
July 2	Cavite	Cavite	Aug. 31	Oct. 26	28
July 3	San Luis	Pampanga			105
July 8	Macabebe	do	July 8	Aug. 18	84
July 3	Mariquina	Rizal		Aug. 3	15
July 4	Hagonoy	Bulacan	July 15	Nov. 23	88
July 5	San Pedro Tunasan	Rizal		July 26	26
July 6	Lilio	La Laguna		July 10	2
July 6	Cabuyao	do	Aug. 16	Sept. 2	88
July 6	Calamba	do		Sept. 4	51
July 7	Bay	do		July 7	1
July 7	San Isidro	Nueva Ecija	Aug. 5	Sept. 3	70
July 7	Taguig	Rizal			43
July 7	Antipolo	do		July 27	3
July 7	Morong	do			22
July 8	Calumpit	Bulacan	Aug. 4	Oct. 1	55
July 8	Bulacan	do	July 15	Oct. 10	40
July 9	Polo	do	July 25	Sept. 22	82
July 9	Angat	do			101
July 9	Santa Rita	Pampanga	July 14		58
July 10	Bacolor	do		Sept. 1	231
July 10	Apalit	do		Sept. 1	55
July 10	Candaba	do			49
July 10	Guagua	do			164

TABLE IV.—*Cholera statistics arranged in the order in which the towns became infected*—Continued.

FISCAL YEAR 1906-1907—Continued.

Date of first case.	Town.	Province.	Highest number of cases.	Date of last case.	Total number of cases.
1906.			1906.	1906.	
July 10	Meycauayan	Bulacan	July 25		30
July 11	Baliuag	do	Aug. 2	Oct. 22	413
July 11	Paombong	do	July 11	Oct. 11	29
July 12	Santa Maria	do			35
July 12	Naic	Cavite	July 19	Oct. 15	63
July 13	Rosario	do	Aug. 22		10
July 13	Pañgil	La Laguna			5
July 13	Malabon	Rizal	July 25	Dec. 28	170
July 13	San Miguel	Bulacan	July 19	Sept. 29	81
July 14	Bocaue	do	July 14	Sept. 26	74
July 14	Angeles	Pampanga			7
July 14	Santa Rosa	La Laguna			54
July 16	Lubao	Pampanga			77
July 16	San Fernando	do			98
July 16	Santo Tomas	do		July 16	1
July 16	Rosales	Pangasinan			4
July 18	Bayambang	do			20
July 18	Imus	Cavite	July 25	Oct. 15	43
July 19	Biñang	La Laguna			22
July 19	Mexico	Pampanga		Nov. 15	17
July 20	Porac	do			17
July 20	Maragondon	Cavite	July 20	Aug. 18	5
July 20	San Jose Guimba	Nueva Ecija		July 20	2
July 21	Cabanatuan	do		Sept. 28	58
July 23	Pagbilao	Tayabas	July 29	Sept. 12	51
July 25	Arayat	Pampanga			58
July 26	Lucena	Tayabas	Aug. 22	Sept. 21	46
July 26	Tarlac	Tarlac	Aug. 5	Aug. 12	14
July 27	Binangonan	Rizal		Aug. 15	20
July 28	Bautista	Pangasinan	Aug. 15	Sept. 10	23
July 29	Peñaranda	Nueva Ecija	Aug. 3	Nov. 13	150
July 29	San Antonio	do	Aug. 4	Sept. 3	20
July 29	Laguimanoc	Tayabas		Aug. 4	7
July 29	Tiaong	do			8
July 30	Floridablanca	Pampanga			16
Aug. 2	Gapan	Nueva Ecija	Aug. 11	Oct. 27	139
Aug. 2	Aliaga	do		Sept. 26	218
Aug. 2	Majayjay	La Laguna			3
Aug. 3	Nagcarlang	do		Sept. 19	66
Aug. 3	Tayabas	Tayabas		Aug. 27	10
Aug. 3	Victoria	Tarlac	Sept. 8	Sept. 25	24
Aug. 3	Caloocan	Rizal			37
Aug. 7	Siniloan	La Laguna			5
Aug. 7	Noveleta	Cavite			27
Aug. 12	Pozorrubio	Pangasinan		Aug. 12	1
Aug. 15	Baguio	Benguet		Aug. 15	1
Aug. 16	Sariaya	Tayabas		Oct. 14	10
Aug. 16	San Francisco de Malabon	Cavite		Sept. 30	4
Aug. 17	Dagupan	Pangasinan			2

TABLE IV.—*Cholera statistics arranged in the order in which the towns became infected*—Continued.

FISCAL YEAR 1906-1907—Continued.

Date of first case.	Town.	Province.	Highest number of cases.	Date of last case.	Total number of cases.
1906.			1906-7.	1906-7.	
Aug. 18	Orion	Bataan			7
Aug. 19	Calasiao	Pangasinan			1
Aug. 25	Pura	Tarlac	Aug. 30	Nov. 8	25
Aug. 25	Talavera	Nueva Ecija	Sept. 16	Oct. 12	108
Aug. 28	Camp Vicars	Moro			9
Sept. 1	Cabatuan	Iloilo	Oct. 2	Oct. 29	366
Sept. 3	Magdalena	La Laguna			5
Sept. 4	Iloilo	Iloilo	Sept. 12	Oct. 21	74
Sept. 11	Moncada	Tarlac		Sept. 12	2
Sept. 14	Binmaley	Pangasinan	Sept. 15		10
Sept. 16	Mabalacat	Pampanga			1
Sept. 18	Dumangas	Iloilo	Sept. 16	Oct. 31	210
Sept. 18	Molo	do			3
Sept. 18	Pavia	do	Sept. 25	Oct. 27	32
Sept. 18	La Paz	do	Sept. 25	Oct. 22	50
Sept. 18	Barotac Nuevo	do		Nov. 2	46
Sept. 19	Jaro	do	Sept. 28	Oct. 13	58
Sept. 21	San Mateo	Rizal		Sept. 21	1
Sept. 21	Nabalas	Iloilo		Sept. 23	6
Sept. 23	Tayug	Pangasinan	Oct. 4	Oct. 15	14
Sept. 24	Los Baños	La Laguna			1
Sept. 25	Igbaras	Iloilo		Sept. 29	2
Sept. 25	Buenavista	do			4
Sept. 27	Miagao	do	Oct. 8	Nov. 8	294
Sept. 29	Guimbal	do			2
Oct. 4	Alimodian	do	Oct. 17	Nov. 5	275
Oct. 8	San Miguel	do	Oct. 17	Nov. 4	195
Oct. 8	Santa Barbara	do		Oct. 27	36
Oct. 8	Leon	do	Oct. 26	Nov. 2	83
Oct. 9	Janiuay	do	Oct. 11	Nov. 16	100
Oct. 9	Banate	do		Oct. 18	12
Oct. 20	Sual	Pangasinan			2
Oct. 27	Camiling	Tarlac	Nov. 3	Nov. 23	26
Oct. 28	Talisay	Occidental Negros		Nov. 19	4
Oct. 28	Silay	do		Dec. 11	7
Nov. 3	Dumarao	Capiz	Nov. 16	Jan. 18	88
Nov. 13	Laguan	Samar		Dec. 22	1
Nov. 13	San Miguel	do			12
Nov. 13	Catubig	do			16
Nov. 22	Dao	Capiz		Jan. 8	15
Nov. 22	Pontevedra	Occidental Negros		Feb. 23	41
Dec. 1	Dumalag	Capiz		Jan. 8	31
Dec. 5	Jamindan	do	Jan. 22	Jan. 26	31
Dec. 8	Palapag	Samar		Mar. 23	42
Dec. 8	Laoang	do			4
Dec. 9	Panay	Capiz			35
Dec. 10	Jinigaran	Occidental Negros		Feb. 23	14
Dec. 23	Pambujao	Samar			3
Dec. 23	Capiz	Capiz		Feb. 16	23
Dec. 27	Tagabiran	Samar		Dec. 27	2

TABLE IV.—*Cholera statistics arranged in the order in which the towns became infected*—Continued.

FISCAL YEAR 1906-1907—Continued.

Date of first case.	Town.	Province.	Highest number of cases.	Date of last case.	Total number of cases.
1907.			1907.	1907.	
Jan. 2	Mambusao	Capiz	Jan. 11	Jan. 26	26
Feb. 13	Saravia	Occidental Negros		Feb. 20	9
Feb. 26	Sigma	Capiz		Jan. 29	2
Mar. 12	Pilar	Occidental Negros		Mar. 16	9
Mar. 23	Bacolod	do		Mar. 23	2
Apr. 7	Victoria	do		Apr. 29	15
	Parañaque	Rizal			25
	Pililla	do			28
	Navotas	do			140
	Bacoor	Cavite			18
	Indang	do			21
	Calawang	La Laguna			1
	Lingayen	Pangasinan			1
	Total number cases				7,085

JULY TO DECEMBER, 1907.

July 22	Carigara	Leyte	Aug. 25	Sept. 8	86
Aug. 9	Mandaon	Masbate	Sept. 12	Oct. 4	53
Aug. 18	Bamgo	Leyte	Sept. 7	Sept. 13	10
Oct. 6	Baliuag	Bulacan	Nov. 15	Dec. 11	10
Nov. 3	Calumpit	do	Nov. 30	Dec. 7	16
Nov. 10	San Miguel	do	Dec. 6	Dec. 10	26
Nov. 14	Guagua	Pampanga	Dec. 14	Dec. 14	24
Nov. 14	Sexmoan	do	Dec. 8	Dec. 12	42
Nov. 19	Santa Rita	do	Nov. 19	Dec. 5	4
Nov. 26	México	do	Nov. 26	Nov. 26	1
Nov. 29	Apalit	do		Dec. 11	9
Nov.	Bacolor	do	Dec. 7	Dec. 13	46
Nov.	San Fernando	do	Dec. 12	Dec. 14	10
Nov.	Macabebe	do	Dec. 6	Dec. 12	52
Nov.	Betis	do		Dec. 8	4
Nov.	San Luis	do	Dec. 6	Dec. 6	2
Dec. 1	Orion	Bataan	Dec. 1	Dec. 4	2
Dec. 1	Lubao	Pampanga	Dec. 15	Dec. 31	27
Dec. 2	Paombong	Bulacan	Dec. 10	Dec. 11	18
Dec. 2	Quingua	do	Dec. 7	Dec. 10	3
Dec. 2	Bulacan	do	Dec. 4	Dec. 7	2
Dec. 2	Mabalacat	Pampanga	Dec. 2	Dec. 2	1
Dec. 3	Candaba	do	Dec. 3	Dec. 3	1
Dec. 4	Hagonoy	Bulacan	Dec. 4	Dec. 4	3
Dec. 4	Bocaue	do	Dec. 5	Dec. 10	5
Dec. 10	Balanga	Bataan	Dec. 10	Dec. 10	1
Dec. 23	Malolos	Bulacan	Dec. 10	Dec. 11	7
	Florida	Pampanga			3
	Minalin	do			8
	Caloocan	Rizal			6
	Malabon	do			1
	Total				478

TABLE II.—*Cases and deaths from cholera in the city of Manila, January 1, 1906, to January 1, 1907.*

BY AGES.

Age.	Cases.	Deaths.	Mortality.
Under 30 days	1	1	100
1 month to 2 years	39	36	92.3
2 to 5 years	121	116	95.9
5 to 10 years	54	50.	92.6
10 to 15 years	56	43	76.8
15 to 20 years	97	75	77.3
20 to 25 years	112	96	85.7
25 to 30 years	113	100	97.4
30 to 35 years	71	57	80.3
35 to 40 years	61	55	90.2
40 to 45 years	24	22	91.3
45 to 50 years	35	32	91.4
50 to 55 years	18	17	94.4
55 to 60 years	22	22	100
60 to 65 years	5	5	100
65 to 70 years	11	11	100
70 to 75 years	2	1	50
75 to 80 years	3	3	100
80 to 85 years	1	0	0
85 to 90 years	2	2	100
Over 90 years			
Total	848	744	87.7

BY RACE.

Race.	Cases.	Deaths.	Mortality.	1 case to—	Date last case.
Americans	12	9	75	488	Sept. 4, 1906
Filipinos	782	698	89.3	243	Nov. 17, 1906
Chinese	30	27	90	741	Oct. 12, 1906
Foreigners	24	10	41.7	189	Nov. 27, 1906

TABLE III.—*Cases and deaths from cholera in the city of Manila, January 1, 1907, to January 1, 1908.*

BY AGES.

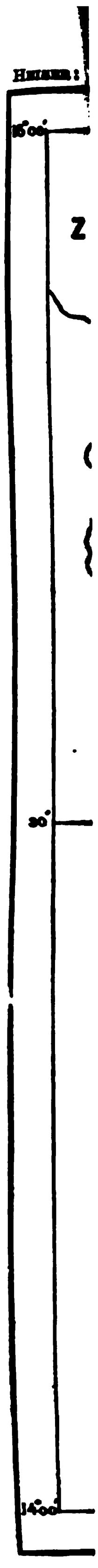
Age.	Cases.	Deaths.	Mortality.
Under 30 days			
1 month to 2 years	6	6	100
2 to 5 years	14	13	92.85
5 to 10 years	15	14	93.33
10 to 15 years	12	10	83.33
15 to 20 years	21	14	66.66
20 to 25 years	30	28	93.33
25 to 30 years	40	32	80
30 to 35 years	26	24	92.30
35 to 40 years	21	20	95.23
40 to 45 years	16	13	81.25
45 to 50 years	8	8	100
50 to 55 years	7	7	100
55 to 60 years	3	1	33.33
60 to 65 years	2	2	100
65 to 70 years	2	2	100
70 to 75 years			
75 to 80 years			
80 to 85 years			
85 to 90 years			
Over 90 years			
Total	223	194	86.99

BY RACE.

Race.	Cases.	Deaths.	Mortality.	1 case to—	Date last case.
Americans	3	0	0.0	1,733	Oct. 17, 1907
Filipinos	212	186	87.7	921	Dec. 31, 1907
Chinese	4	4	100	4,507	Oct. 19, 1907
Foreigners	4	4	100	1,255	Oct. 9, 1907
Total	223	194	86.9	1,002	

ILLUSTRATIONS.

PLATES I AND II. Houses in the Farola district where cholera first appeared in 1902.
MAP No. 1. Portion of Philippines including Manila Bay and Laguna de Bay.
2. The Philippine Islands, by provinces.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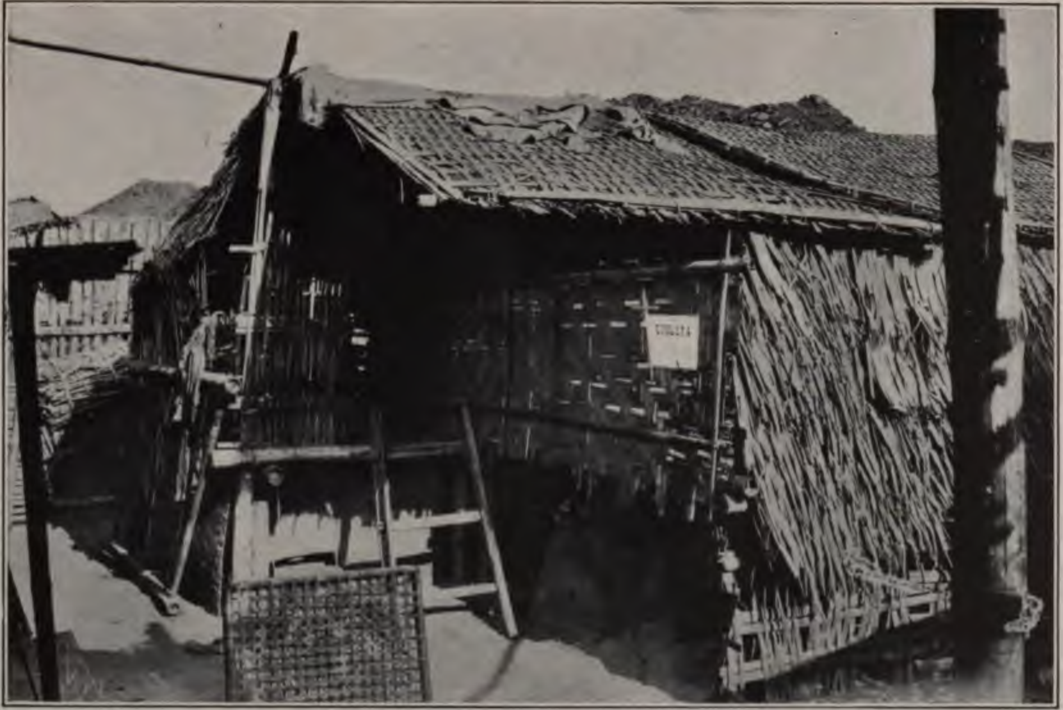

PLATE II. HOUSES IN THE FAROLA DISTRICT WHERE CHOLERA FIRST APPEARED IN 1902.

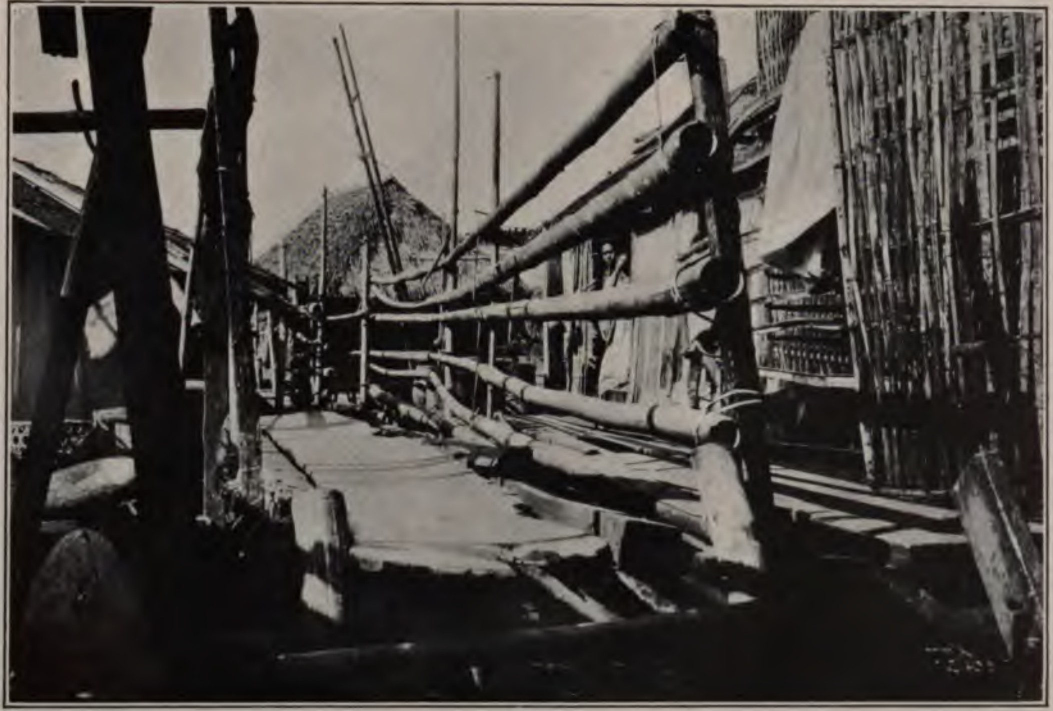

PLATE I. HOUSES IN THE FAROLA DISTRICT WHERE CHOLERA FIRST APPEARED IN 1902.

STUDIES OF CHOLERA.[1]

By Harry T. Marshall.
(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

I. VARIATIONS IN VIRULENCE.

During the past year or more we have been continuing the studies of cholera at this laboratory, previous reports upon this subject having been published by Dr. Strong. In this paper I will review the results obtained up to the present time.

The experiments which I have conducted were undertaken with the view of continuing certain investigations upon the variation of bacteria with special reference to their so-called immunization. This research was begun a few years ago with the dysentery bacillus.[2] At that time we came to the conclusion that selection and variation are constantly manifesting their action upon bacteria, and that these processes probably play an important part, not only in the rise of epidemics, but also in the development of each individual case of an infectious disease, in such a manner that in a case of infection a large number of the bacteria are killed by the host, while a relatively small number become adapted to their environment, survive, multiply and produce the disease. At that time, we were able by growing the dysentery bacillus upon media containing anti-dysenteric serum, to develop a variety of bacillus which not only was not agglutinated or impeded in its growth by the antiserum, but which actually flourished more luxuriantly in the presence of the serum than it did under other conditions and which no longer united with the agglutinins in specific antidysenteric serum. A preliminary attempt was made in this laboratory to repeat the same experiment with the cholera vibrio. Two or three stock cultures were inoculated into bouillon or peptone solutions containing small amounts of anticholera serum and after intervals varying from a day up to a week or more, transplants were made into fresh flasks of bouillon containing anticholera serum. As many as ten successive transplants in one series were made after this fashion, but the cholera vibrio did not lose its capacity to become agglutinated, although it grew readily in the new medium. This line of investigation was not carried any further.

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[1] Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, February 28, 1908.

[2] Marshall and Knox: *J. Med. Research* (1906), N. S. 10, 325.

One interesting observation was made upon a strain which had been transplanted nine times through successive serum bouillon cultures and which had been allowed to remain in the last flask for a long period. The vibrio was plated out and its biological characteristics determined. Among other distinctive features the blood-agar-hæmolysis test was tried simultaneously with this bacterium and the stock culture from which it was taken for the original transplant into serum. The original stock culture showed no hæmolysis within twenty-four hours and only a trace in forty-eight hours, while the vibrio which had been grown in beef broth, containing anticholera horse serum, showed a marked ability to produce hæmolysis of goat's blood within twenty-four hours. We have here a definite variant produced by artificial laboratory means, the only difference between the stock culture and the variant being that the variant grew in the presence of serum from a horse which had been immunized against cholera. The factor which produced the hæmolyzing reaction was probably not the specific anticholera substance of the serum but those constituents of it which are close to the ones of the red blood corpuscles.

The question of variation was then attacked in a different way by Dr. Philip K. Gilman, of the Philippine Medical School, and myself. We created an artificial epidemic of cholera in guinea pigs in order to observe what changes the vibrio would undergo both in virulence and in other respects. A guinea pig received an inoculation intraperitoneally of 0.1 cubic centimeter of the material taken from the ileum of a man dead of cholera, the diagnosis being based upon clinical history, autopsy appearances and laboratory examinations. The guinea pig died within twenty-four hours; 0.1 cubic centimeter of the peritoneal contents from this animal, diluted with salt solution, was inoculated into the peritoneal cavity of a second guinea pig, and upon its death, within twenty-four hours, the peritoneal exudate was used for inoculating a third. Upon its death within twenty-four hours, the exudate was diluted and a series of guinea pigs was inoculated with varying amounts of this material. The minimum dose fatal within twenty-four hours was 0.02 cubic centimeter. The exudate from the guinea pig killed by this amount was diluted and a fresh series inoculated. On this occasion, although as small a dose as 0.0005 cubic centimeter was inoculated, the minimal fatal dose was not determined. The exudate from the animal killed by the lowest fatal dose was used for inoculating a sixth series and in this 0.0001 cubic centimeter was the minimal fatal dose. From the exudate obtained from the animal which succumbed to this quantity a new series was inoculated and 0.00002 cubic centimeter proved fatal. An interesting result followed the next inoculation. The exudate was diluted and inoculated as usual, but none of the guinea pigs died within twenty-four hours, although the doses inoculated varied from 0.001 to 0.00001 cubic centimeter. In other words, the virulence had suddenly fallen at least to one-fiftieth of its former strength, and how much more is not known. It is important to determine the nature of the biological processes associated with this sudden abatement of virulence, but the only clue furnished by this series is that 1 cubic centimeter of a 1 to 1,000,000 dilution of the exudate from the next to the last guinea pig of the series, when plated in agar, contained colonies too numerous to count, so that at least it is clear that the bacteria had not lost their viability. We may account for the sudden loss of virulence either by supposing that the power of toxin formation suddenly disappeared, or that the ability of the bacteria to resist bactericidal action suddenly failed them. It seems clear that there was a sufficient number of surviving bacteria carried over from the next to last guinea pig; this was shown by the results of plating. The results of this series of inoculations are shown in Series I, and the sudden rise and fall in virulence is charted in fig. 1.

The strain of cholera which has just been described was obtained from an autopsy during the height of a small epidemic. Several other attempts were made to repeat this result subsequently, when the epidemic was on the wane, both with strains of cholera inoculated into guinea pigs directly from the intestine and with laboratory stock cultures. The results are shown in Series II, III, IV, V, and VI and in figs. 2–5. It is seen that no strain was obtained, the virulence of which could be increased so successfully and regularly as that of the first.

Turning to Series II, we find the results are less regular, although here again there was a gradual rise in virulence up to a fatal dose of 0.0001 cubic centimeter. The irregularities are difficult to explain. For instance, we find on November 11 that 0.0002 cubic centimeter is fatal, while 0.001 is not so. Again, on November 13 neither 0.01 nor 0.0002 cubic centimeter killed the animal, while 0.0001 and 0.001 did so. It is possible that this difference can be explained upon a physical basis, for the exudate was tenacious and possibly did not spread evenly throughout the diluting salt solution.

The virulence was irregular in Series III also. An observation made in this series throws some light upon the mechanism of the fall of an epidemic. In the fifteenth inoculation made on November 28, the only animal which died within twenty-four hours received 0.01 cubic centimeter of exudate. This animal did not die until 10.15 on the morning of November 29. The autopsy was performed at once and 0.25 cubic centimeter of tenacious, yellowish, cloudy exudate was recovered from the peritoneal cavity. As the table shows, the animals inoculated with this exudate did not die within twenty-four hours. At the same time 1 cubic centimeter of a 1 to 80 dilution of this exudate was inoculated

SERIES I.—*From cholera autopsy, September 4, 1907, contents of ileum direct into guinea pig intraperitoneally.*

[+ = fatal in 24 hours after inoculation. 0 = not fatal in 24 hours after inoculation.]

Date of inoculation.	Volume (in fractions of a cubic centimeter) of exudate from dead guinea pigs which proves fatal in less than 24 hours after intraperitoneal inoculation into a new set of guinea pigs.														Appearance of exudate.	Cultures, smears, etc., from exudate.	Remarks.
	0.2.	0.1.	0.05.	0.02.	0.01.	0.005.	0.002.	0.001.	0.0005.	0.0002.	0.0001.	0.00005.	0.00002.	0.00001.			
Sept. 4	----	+[a]	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Sept. 5	----	+	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Sept. 6	----	+	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Sept. 7	+	+	+	+	0	0	0	0	0	----	----	----	----	----	----	----	
Sept. 8	----	----	----	+	+	+	+	+	+	----	----	----	----	----	----	----	0.0005 cc. fatal in less than 24 hours; minimum fatal dose not reached.
Sept. 9	----	----	----	----	----	----	----	----	+	+	+	0	0	0	4 cc. of thick tenacious exudate.	1 cc. of 1 to 100,000 dilution plated in agar; colonies too numerous to count.	
Sept. 10	----	----	----	----	----	----	----	+	([b])	([b])	+	+	+	0	0.00002 has 1.5 cc. thick tenacious exudate.	1 cc. of 1 to 1,000,000 dilution plated in agar; colonies too numerous to count.	
Sept. 11	----	----	----	----	----	----	----	0	([b])	([b])	([a])	0	0	0	----	----	

[a] A second guinea pig receiving 0.1 cubic centimeter of bowel contents did not die until the third day.

[b] Not inoculated.

September 7, 1907, was the first day upon which a series of several guinea pigs was inoculated.

of this laboratory and I, noted that during the height of the epidemic the vibrios presented the typical morphology, were actively motile and agglutinated in a high dilution of serum; while toward its close the curves of the vibrios became less evident, many forms were found with little or no curve, and the bacteria in general were slenderer and longer; the motility diminished greatly and the movement, if present at all, was very sluggish, while the agglutinatibility remained practically constant. In two patients who recovered from cholera, examined at the close of this epidemic, the vibrios remained in the stools after convalescence; in one case for four or five days, while in the other they were still present after ten days, when the patient left the hospital and was lost sight of. The importance of this occurrence in its bearing upon the spread of cholera is sufficiently evident to make comment superfluous. This case recalls at once the findings of Ruffer and Gotschlich, which will be discussed in a later section of this report.

The study of the bacterial variation occurring among cholera vibrios is being pursued along other lines also. A number of different strains of cholera and cholera-like vibrios have been collected and a comparison is being made of their pathogenicity, motility, morphological and cultural characteristics, serum reactions, and ability to form toxins. The results of these studies will be reported later. Up to the present time the chief attention has been devoted to noting the cultural characteristics, and there is evidence of appreciable differences in the manner of growth of the various organisms which are being examined.

SERIES I.—*From cholera autopsy, September 4, 1907, contents of ileum direct into guinea pig intraperitoneally.*

[+ = fatal in 24 hours after inoculation. 0 = not fatal in 24 hours after inoculation.]

Date of inoculation.	Volume (in fractions of a cubic centimeter) of exudate from dead guinea pigs which proves fatal in less than 24 hours after intraperitoneal inoculation into a new set of guinea pigs.														Appearance of exudate.	Cultures, smears, etc., from exudate.	Remarks.
	0.2.	0.1.	0.05.	0.02.	0.01.	0.005.	0.002.	0.001.	0.0005.	0.0002.	0.0001.	0.00005.	0.00002.	0.00001.			
Sept. 4	----	+[a]	----	----	----	----	----	----	----	----	----	----	----	----	----------	----------	
Sept. 5	----	+	----	----	----	----	----	----	----	----	----	----	----	----	----------	----------	
Sept. 6	----	+	----	----	----	----	----	----	----	----	----	----	----	----	----------	----------	
Sept. 7	+	+	+	+	0	0	0	0	0	----	----	----	----	----	----------	----------	
Sept. 8	----	----	----	+	+	+	+	+	+	----	----	----	----	----	----------	----------	0.0005 cc. fatal in less than 24 hours; minimum fatal dose not reached.
Sept. 9	----	----	----	----	----	----	----	----	+	+	+	0	0	0	4 cc. of thick tenacious exudate.	1 cc. of 1 to 100,000 dilution plated in agar; colonies too numerous to count.	
Sept. 10	----	----	----	----	----	----	----	+	([b])	([b])	+	+	+	0	0.00002 has 1.5 cc. thick tenacious exudate.	1 cc. of 1 to 1,000,000 dilution plated in agar; colonies too numerous to count.	
Sept. 11	----	----	----	----	----	----	----	0	([b])	([b])	([a])	0	0	0	----------	----------	

[a] A second guinea pig receiving 0.1 cubic centimeter of bowel contents did not die until the third day.

[b] Not inoculated.

September 7, 1907, was the first day upon which a series of several guinea pigs was inoculated.

SERIES II.—*Inoculations started from a 24-hour bouillon culture of a stock laboratory culture of cholera.*

[+ = fatal within 24 hours after inoculation. 0 = not fatal within 24 hours after inoculation.]

Date of inoculation.	Volume (in fractions of a cubic centimeter) of exudate from dead guinea pigs which proves fatal in less than 24 hours after intraperitoneal inoculation into a new set of guinea pigs.														Appearance of exudate and peritoneal surfaces.	Cultures, smears, etc., from exudate.	Remarks.
	0.5.	0.1.	0.05.	0.02.	0.01.	0.005.	0.002.	0.001.	0.0005.	0.0002.	0.0001.	0.00005.	0.00002.	0.00001.			
Oct. 30	+	0	0	0	0	----	----	----	----	----	----	----	----	----	12 cc. turbid yellow mucoid exudate.		Fatal dose of *stock cholera culture*.
Nov. 6	----	----	----	----	----	----	----	----	----	----	----	----	----	----	Hæmorrhagic exudate.		Received 2 cc. of peptone culture from exudate Oct. 30.
Nov. 7	----	+	----	----	----	----	----	----	----	----	----	----	----	----	Injected peritoneum; fibrin flakes; 1 cc. turbid bloody exudate.		
Nov. 8	----	+	+	+	0	0	+	0	0	----	----	----	----	----	0.002 guinea pig contains 1½ cc. bloody peritoneal exudate.		Guinea pig dying after a dose of 0.002 was pregnant.
Nov. 9	----	----	----	+	----	0	0	0	+	+	----	----	----	----	Petechiæ over colon; a few fibrin flakes over peritoneum; turbid red exudate.		
Nov. 10	----	----	----	----	+	+	----	0	----	0	0	0	0	----			
Nov. 11	----	----	----	----	+	----	----	0	----	+	0	0	0	----			
Nov. 12	----	----	----	----	+	----	----	+	0	0	0	0	----	----	Slight rosy coloration; peritoneal cavity almost dry: no fibrin: no extravasation.	Plates and slants show pure culture slightly curved rods.	
Nov. 13	----	----	----	----	0	----	----	+	----	0	+	0	0	----	3½ cc. bright red tenacious fluid.	Peptone gives general turbidity and sediment.	Plates, and slants apparently pure culture of slightly curved rods.
Nov. 14	----	----	----	----	+	----	----	0	----	+	0	0	0	----	5 cc. turbid bloody fluid.	No surface growth on peptone.	No growth in alkaline agar plates. Series discontinued.

Series III.—*Inoculation made from the bowel contents of a fatal case of cholera directly into peritoneal cavity of guinea pig.*

[+ = fatal within 24 hours after inoculation. 0 = not fatal in 24 hours after inoculation.]

Date of inoculation.	Volume (in fractions of a cubic centimeter) of exudate which proved fatal within 24 hours after intraperitoneal inoculation into guinea pigs.														Appearance of exudate and peritoneal surfaces.	Cultures, smears, etc., from exudate.	Remarks.
	0.2.	0.1.	0.05.	0.02.	0.01.	0.005.	0.002.	0.001.	0.0005.	0.0002.	0.0001.	0.00005.	0.00002.	0.00001.			
Nov. 14															5 cc. turbid yellow exudate, large flakes of fibrin over peritoneal surfaces.		1 cc. of bowel content from fatal case cholera inoculated intraperitoneally.
Nov. 15		+			+			0			0		0		0.2 cc. reddish fluid. Injected peritoneum; fibrin flakes.		
Nov. 16		+	+														Not enough exudate for further dilutions.
Nov. 17					+			+		+	0	0	0		4 cc. turbid yellow viscous fluid fibrin.	Plates; apparently pure culture cholera.	
Nov. 18					+			0		0	0	0	0		8 cc. blood-stained fluid	Peptone; no pellicle; plates, slants, morphology = pure cholera vibrios with definite comma curve in over 50 per cent.	
Nov. 19					+			0			0				4.5 cc. bloody turbid exudate	Plates; apparently pure culture cholera.	
Nov. 20					+			+			0				3¼ cc. bloody exudate; fibrin	Peptone and plates apparently pure culture cholera.	
Nov. 21					+			0			0				4 cc. bloody exudate	Plates and slants, pure culture of slender rods about 3 μ with irregular stain; 1 in 10 with curved tip.	
Nov. 22					+			+			0				2 cc. turbid red fluid		
Nov. 23					+			0		0						Peptone not typical	
Nov. 24					+			0		0						do	

Nov. 25	----	----	----	----	+	----	----	+	----	----	+	----	----	----	3½ cc. viscous blood-tinged exudate.	Plates and morphology apparently pure culture cholera; 1 in 8 to 1 in 15 curved.	Limit of virulence not reached.
Nov. 26	----	----	----	----	+	----	----	+	----	----	0	0	0	----	3 to 4 cc. bloody turbid fluid ----	Peptone not typical, i. e., no pellicle.	
Nov. 27	----	----	----	----	+	----	----	0	----	----	+	0	0	0	¼ cc. bloody turbid fluid ----	Peptone gives surface growth ----	
Nov. 28	----	----	----	----	+	----	----	0	----	0	0	0	----	----	¼ cc. yellow very tenacious exudate.	Rods 1 to 3 μ in length; irregular staining, about 1 in 20 show slight curve.	
Nov. 29	----	----	----	----	0	----	----	0	----	----	0	0	0	----	----	----	

Series IV.—*Inoculated from surface growth of peptone culture—24 hours old—from ileum of cholera autopsy.*

[+ = fatal within 24 hours after inoculation. 0 = not fatal in 24 hours after inoculation.]

Date.	Dilutions (in fractions of a cubic centimeter) of peptone culture used for intraperitoneal inoculation of guinea pigs.														Remarks.
	0.2.	0.1.	0.05.	0.02.	0.01.	0.005.	0.002.	0.001.	0.0005.	0.0002.	0.0001.	0.00005.	0.00002.	0.00001.	
Nov. 23	----	0	----	----	0	----	----	0	----	----	----	----	----	----	All animals survived. Series discontinued.

Series V.—*Inoculated intraperitoneally with red gruel-like bowel contents from cholera autopsy.*

[+ = fatal within 24 hours after inoculation. 0 = not fatal in 24 hours after inoculation.]

Date.		Volume (in fractions of a cubic centimeter) of exudate from dead guinea pig which proved fatal within 24 hours after intraperitoneal inoculation into guinea pigs.														Exudate, etc.	Cultures, smears, etc.	Remarks.
		1 cc.	0.1.	0.05.	0.02.	0.01.	0.005.	0.002.	0.001.	0.0005.	0.0002.	0.0001.	0.00005.	0.00002.	0.00001.			
Dec.	5	-	+	----	----	0	----	----	----	----	----	----	----	----	----	¾ cc. viscous fluid; blood tinged	Mixed culture; a few motile curved rods.	Inoculated with contents of ileum.
Dec.	6	----	+	----	----	+	----	----	0	----	0	0	0	----	----	3 cc. yellow viscous substance	A few curved slowly motile rods in exudate.	
Dec.	7	----	+	----	----	0	----	----	0	----	----	0	0	0	----	Semipurulent; not viscous	Mixed culture; no vibrios found.	
Dec.	8	----	0	----	----	+	----	----	0	----	----	0	----	----	----	1¼ cc. slightly tenacious purulent fluid.	1 or 2 curved rods amid about 200 bacteria of various shapes.	
Dec.	9	----	----	----	----	0	----	----	0	----	----	0	----	----	----	----	----	Series discontinued.

Series VI.—*Inoculation from bowel contents from cholera autopsy.*

Date.		Volume of exudate from dead guinea pig which proved fatal within 24 hours after intraperitoneal inoculation into guinea pigs.														Exudate, etc.	Cultures, smears, etc.	Remarks.
		1 cc.	0.1.	0.05.	0.02.	0.01.	0.005.	0.002.	0.001.	0.0005.	0.0002.	0.0001.	0.00005.	0.00002.	0.00001.			
Dec.	6	+	0	----	----	0	----	----	----	----	----	----	----	----	----	3 cc. brownish yellow fluid	Mixed culture; no vibrios seen.	1 cc. of contents of ileum inoculated.
Dec.	7	+	+	----	----	0	----	----	0	----	----	----	----	----	----	1 cc. yellowish slightly tenacious fluid.	Mixed culture with very few sluggish curved rods.	
Dec.	8	----	+	----	----	+	----	----	----	----	----	----	----	----	----	¼ cc. yellow fluid	----	Limit of virulence not reached.
Dec.	9	----	0	----	----	0	----	----	0	----	----	0	----	----	----	----	----	Series discontinued.

ILLUSTRATIONS.

FIG. 1. Chart of the changes in virulence of cholera strain No. 1. (To accompany Series I.)
2. Chart of the changes in virulence of cholera strain No. 2. (To accompany Series II.)
3. Chart of the changes in virulence of cholera strain No. 3. (To accompany Series III.)
4. Chart of the changes in virulence of cholera strain No. 4. (To accompany Series IV.)
5. Chart of the changes in virulence of cholera strain No. 5. (To accompany Series V.)

Figure I.

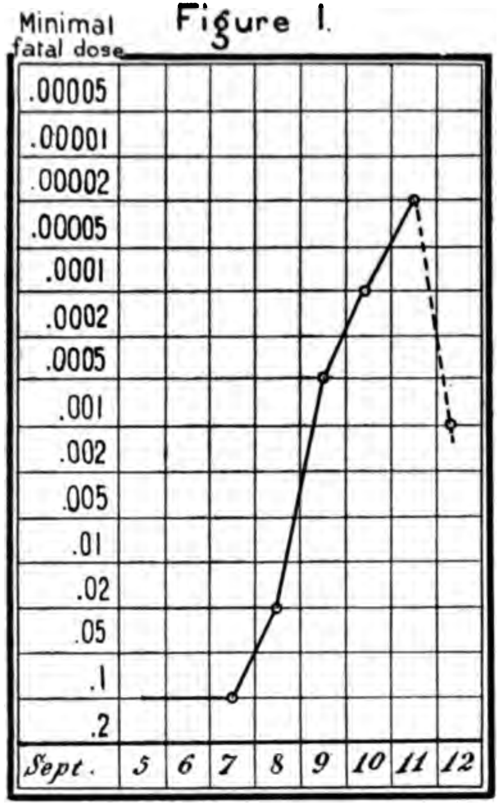

Chart of the changes in virulence of cholera strain No. 1. (To accompany Series I.)

Figure II.

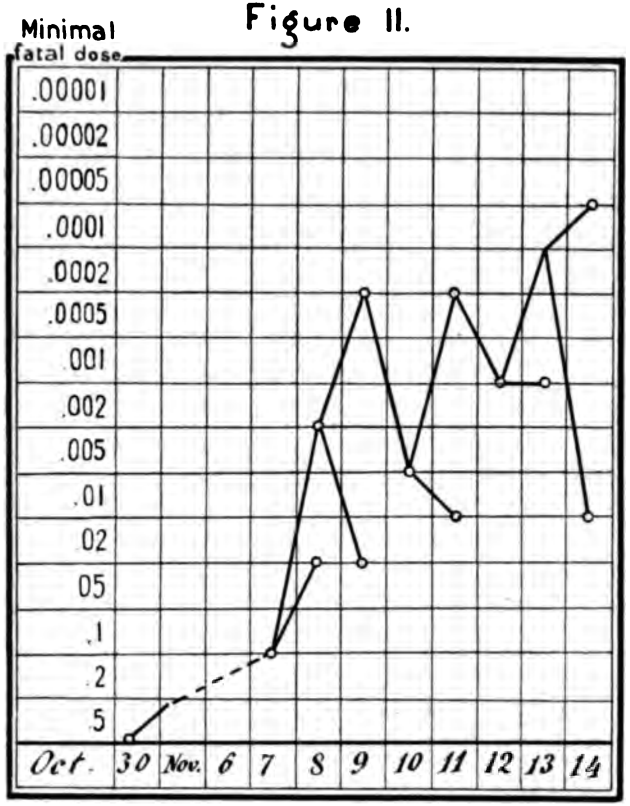

Chart of the changes in virulence of cholera strain No. 2. (To accompany Series II.)

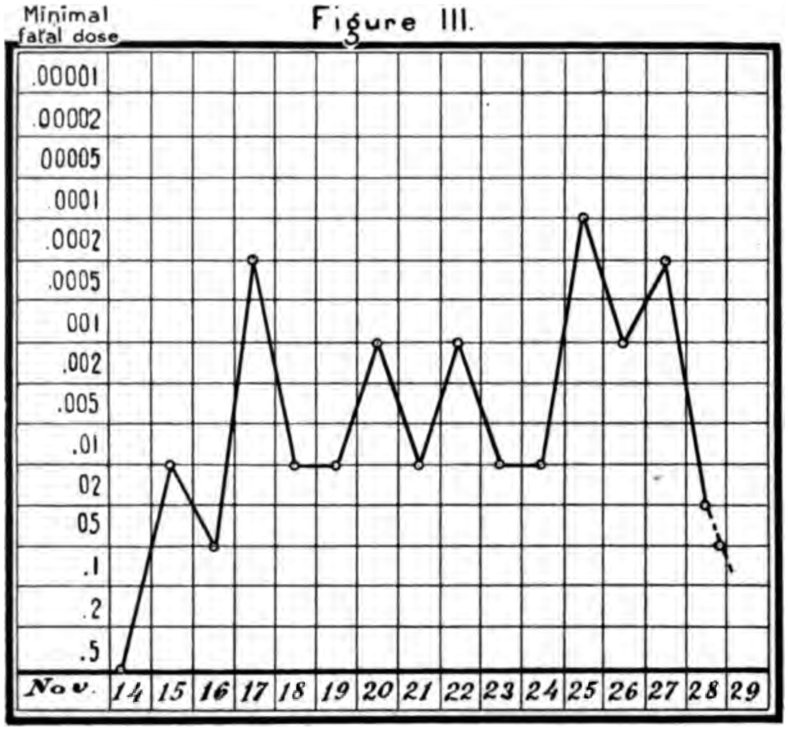

CHART OF THE CHANGES IN VIRULENCE OF CHOLERA STRAIN No. 3. (To accompany Series III.)

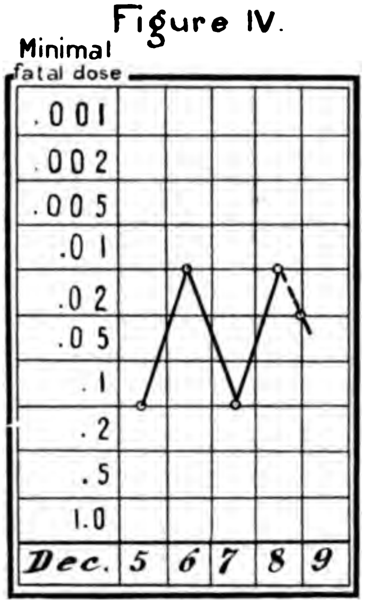

CHART OF THE CHANGES IN VIRULENCE OF CHOLERA STRAIN No. 4. (To accompany Series IV.)

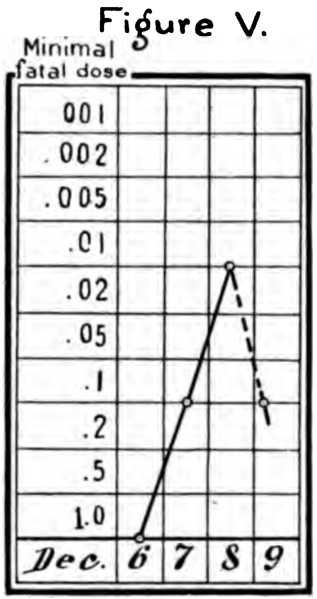

CHART OF THE CHANGES IN VIRULENCE OF CHOLERA STRAIN No. 5. (To accompany Series V.)

A BIOLOGICAL STUDY OF THE WATER SUPPLY OF THE PHILIPPINE ISLANDS, WITH A DESCRIPTION OF A NEW PATHOGENIC ORGANISM.[1]

By Ralph T. Edwards.

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

Manila at present is preparing to obtain an ample supply of drinking water and at the same time the city is very commendably applying itself to the task of making that supply safe. What will eventually be accomplished in this undertaking can be understood best by a study of the waters of the Islands, and therefore the statistics found in the official reports of water examinations made by the Bureau of Science up to January 1, 1908, are of great importance. These reports include waters from various places in the Islands and from divers sources in and about Manila; they include some 700 examinations made by Doctors Wherry, Woolley, Herzog, Bowman and Edwards, and by Messrs. Clegg and Willyoung.

This paper concerns itself first with the examination of waters from the *esteros* [2] because of the fact that while these are probably never drunk by the people here, laundry work is done on the estero banks and it is probable that dishes and cooking utensils are occasionally washed in those estuaries the odor of which is not too offensive. Examinations of flavoring extracts, soda water and bottled lemonade are also included for obvious reasons.

I have also taken up the subject of river water because our present supply for the city of Manila is derived from the Mariquina River, which flows into the Pasig some 6 miles above the mouth of the latter, and various other sources for drinking water are also included because of the reputation for purity which they enjoy in various places other than this city.

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[1] Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, February 29, 1908.

[2] Esteros are arms of the deltas of the Philippine rivers which are subject to tidal fluctuations and which are filled with salt water at high tide and are brackish at ebb tide. A number of these estuaries ramify through the city of Manila, the houses of the people are close to the banks and traffic crosses them by bridges. They are used by lighters, boats and other small craft. The current is sluggish.

Fifty-three per cent of all the 700 waters have been condemned for one cause or another. (See Chart I.) Of the total number examined, amœbæ were present in 39.4 per cent, but there were 46 per cent positive in those reports in which it was specifically stated that these organisms were searched for;[3] flagellata were encountered in 20 per cent of all waters, and the percentage of positive results on the reports in which these organisms are entered is 23.5; ciliata were mentioned as being present in 7.5 per cent and of the number in which protozoa were stated as being present or not, in 9.5 per cent; protozoa, without specification of identity, were mentioned in 1 per cent of all the waters and in 1.16 per cent of the number of completed examinations in which mention is made of such animal forms. High bacterial count was given as a reason for condemning a water in 9.3 per cent. However in 43 per cent of those cases where the fact of making such a count was mentioned, pathogenic bacteria were present in 0.83 per cent of the total, and in 28 per cent of all the cases in which a specific examination for these organisms was mentioned. Numerous special examinations for the presence of the cholera vibrio were undertaken, but up to January 1, 1908, no such specific organism was found, excepting in one estero where a railroad company had been emptying its sewage pails.

Chart II shows the percentage of condemned waters from various sources. The waters from public places included those from the courthouse, the public offices, the prison, restaurants and eating houses, excepting in instances where it was specifically stated that the sample examined was distilled water direct from one of the distilling plants. It is probable that if the number of samples of the latter class were to be subtracted from the total, the percentage of contaminated water would be much higher; as it is, it reaches 55 per cent. Fifty per cent of the spring water was condemned. The Manila supply, including samples from the intake, furnished the highest percentage—namely, 95.7. The study of the examinations from the latter source furnishes one of the strong arguments in favor of sand filtration. The colony count of the water secured from Manila hydrants varied from 40 to 600 bacteria in 1 cubic centimeter water. The low figure might be kept constant with an efficient sand filtration plant.

The samples of water passed through various household filters of divers construction gave 95 per cent to be condemned, the second highest number, but it is well to add that in nearly every instance representatives of this class were reported upon unfavorably because of the presence of animal forms. This result demonstrates the hopelessness of the expectation that a supply secured by filtration should be free from animal forms, but we know that water which has been subjected to slow sand filtration shows a very low number of bacteria and therefore such a process would greatly lessen the danger of *bacterial* infection for those who refuse to sterilize the hydrant water by some means before using it. Some experiments in sand filtration have been carried on in Manila, but these were only in mechanical filtration and left out of account the biological principle upon which all sand filtration should be based. The experiments of Musgrave and Clegg show that amœbæ require some organism to be in symbiosis with them, hence it is not difficult to believe that a reduction in the number of amœbæ would follow a diminution in the number of symbiotic organisms which, in this case, would be the bacteria in the water. It is a disputed point whether or not all amœbæ are pathogenic. If they are not, it would follow that by means of the reduction of the number of bacteria we might eliminate the pathogenic ones and so by the diminution of the total number of amœbæ, escape those which are pathogenic. Aside from this factor we know that natural immunity, or the sterilizing action of a healthy stomach, is able to a certain extent to protect individuals from intestinal bacterial infections. We know that many people in these Islands consistently refuse to sterilize the drinking water which they use, and a much larger number have their dishes washed only in unsterilized tap water.

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[3] That is, reports in which amœbæ are especially mentioned as "positive" or "negative."

Only a few years ago, the prevalence of amœbic dysentery among Europeans was so great as seriously to reflect upon the Islands as a home for the Caucasians. However, the experience then gained was followed by the adoption of great precautions by this part of the population so far as purity of food and water was concerned, but now many persons who have had this experience have left, or have to a slight degree become immune to the ordinary chances of infection and the remainder are correspondingly careless. New arrivals are constantly appearing, and with such changes in the population and with certain other factors which we do not understand, we may probably have another epidemic at some future time, but we can furnish an improvement in the future water supply in the shape of a slow sand filtration plant. This would also probably help in the continual fight against cholera in Manila.

Few samples of waters bottled and for sale have been condemned and these, with one exception, were cheap products sold from low-class shops; only one sample of a reputable brand of water was condemned for high bacterial count, while no other of the same brand of water had even ten bacteria to the cubic centimeter, hence we would conclude that reputable brands of bottled water are safe.

No flavoring extract was condemned and only a few samples of soda water and lemonade, but the number of specimens examined was so small that we should draw no conclusions therefrom.

The specimens from artesian wells gave most satisfactory results, as only 8.5 per cent of the wells were condemned. The high figure 15.8

represents the proportion of samples at first rejected, but in some cases later investigation made with great precautions forced the conclusion that the samples were condemned in the first place because of contamination in securing the specimen.

Wells and cisterns showed 63.3 per cent of rejections and I do not doubt but that this number is far too low, for in instances the request for examination did not specify whether the sample was from an ordinary or an artesian well.

The miscellaneous places mentioned in the table include rivers, esteros, rice paddies, ponds, pools, ditches and tanks. Many of the requests for examination of samples called for only a partial examination for the presence of the cholera organism, and this accounts for the low percentage condemned.

Water should be condemned (*a*) for the presence of animal parasites, (*b*) for the presence of pathogenic bacteria, (*c*) when the count is above 200 bacteria per cubic centimeter.

The specimens of distilled water condemned were almost without exception rejected because of the presence of protozoa. It would, therefore, be legitimate to conclude that, in the handling of water, there is almost as much danger of contamination with protozoa as there is with bacteria and possibly this contamination is accompanied by greater danger to those who use the water for drinking purposes than the other. It is therefore advisable, in order to insure safety of drinking water, to make as few transfers from one receptacle to another as is possible after sterilization. I have already mentioned the good condition of reliable brands of water bottled and for sale, but can not condemn too strongly the handling which is ordinarily given to distilled and other potable waters when secured in large quantities.

A study of the above reports causes me to advocate a triple biological examination of all samples of water as follows:

Twenty-five cubic centimeters of a 10 per cent peptone solution are added to about 225 cubic centimeters of water in a sterile flask (about the amount probably drunk by an individual at one time). The growth should be examined after twenty-four, forty-eight and seventy-two hours, with due precaution against contamination upon opening for the first two examinations. The report should mention amœbæ, flagellata and ciliata.

Two cubic centimeters should be withdrawn with a sterile syringe at the 24-hour examination and injected into the peritoneal cavity of a guinea pig or rabbit; if the animal does not die within forty-eight hours it is quite probable that there are no pathogenic bacteria present. Plates should be made from the original peptone culture, containing 1, 0.1, 0.01 and 0.001 cubic centimeter of suspected water, respectively, and placed in the incubator for forty-eight hours before the colony count is made.

The figures appearing in this paper bring me to the conclusion that tap water, cistern water, ordinary well water, and water only filtered as a means of sterilization should not be used for drinking purposes in the

Philippines, nor in fact any other water excepting that which is known to be safe and is kept in closed sterile receptacles.

It is of interest to note that during the work on waters there was isolated from a specimen of water taken from a well on Calle Cabildo, Intramuros, a pathogenic bacillus of which I have been able to find no description. Its characteristics are as follows:

Bacillus cabildonis, spec. nov., 1908.

It is a single bacillus with a breadth of less than 1 μ, average length about 2 μ. It stains easily with the standard aqueous dyes and takes a polar stain with Z. N. carbol-fuchsin. It is decolorized by Gram's method. No capsule, spores, vacuoles, or crystals have been observed. The organism is actively motile and a facultative anaërobe. Pleomorphism has not as yet been observed. It grows well either at room or body temperature. A greenish fluorescence develops in twenty-four hours on all transparent media. The bacterium grows well on all ordinary media; nutrient broth remains alkaline as far as my observation goes, without the development of odor; milk is not coagulated, digested or acidified nor is an odor developed; no gas is formed with saccharose, glucose, glycerine or lactose; solidified blood serum is not peptonized; the growth on potato is abundant; indol is produced in sugar-free peptone solution; alkali is formed with or without the presence of carbohydrates. Guinea pigs or rabbits inoculated intraperitoneally with one or two drops of a 24-hour broth culture or with the peritoneal exudate of a previously inoculated animal, die in five or six hours with evidences of peritonitis and septicæmia. While this organism has been encountered but once, its extreme pathogenicity for small animals to my mind makes it of sufficient importance to merit description.

SUMMARY.

The presence of protozoa, pathogenic bacteria or a colony count of more than 200 per cubic centimeter being the criterion, 53 per cent of the waters heretofore examined in this laboratory should be condemned.

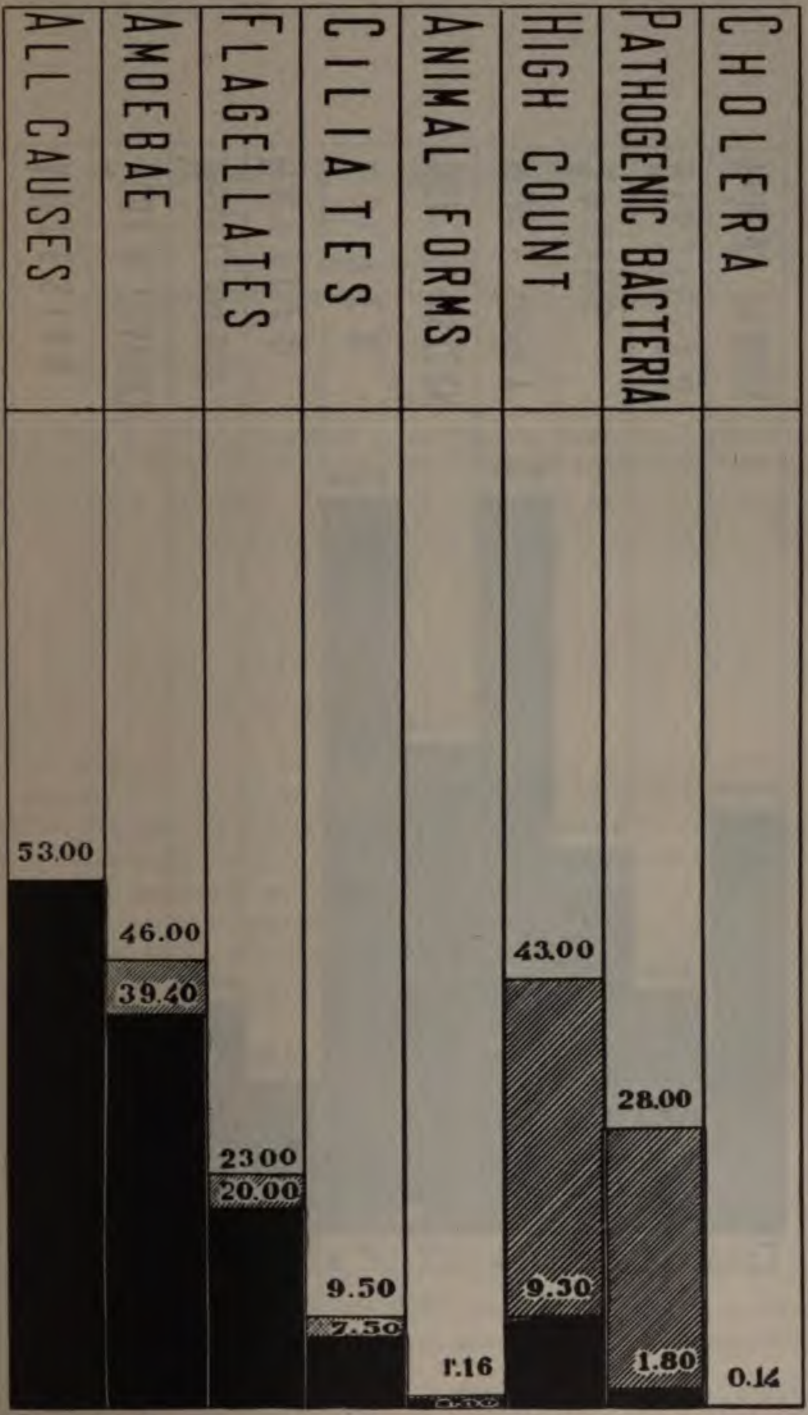
Waters bottled and for sale by reliable firms are safe. The danger of contamination of water with protozoa by handling it is great. This, coupled with the fact that we do not know absolutely what protozoa are pathogenic, makes the use for drinking purposes of all water handled in the ordinary ways, dangerous. All well, cistern, river and hydrant water should be efficiently sterilized and kept in sterile vessels until used.

Not enough careful work has been done on artesian water to justify any general conclusion, but it is safer than any other which is used without being sterilized: it having been repeatedly examined with negative results.

B. cabildonis is described as a new pathogenic species.

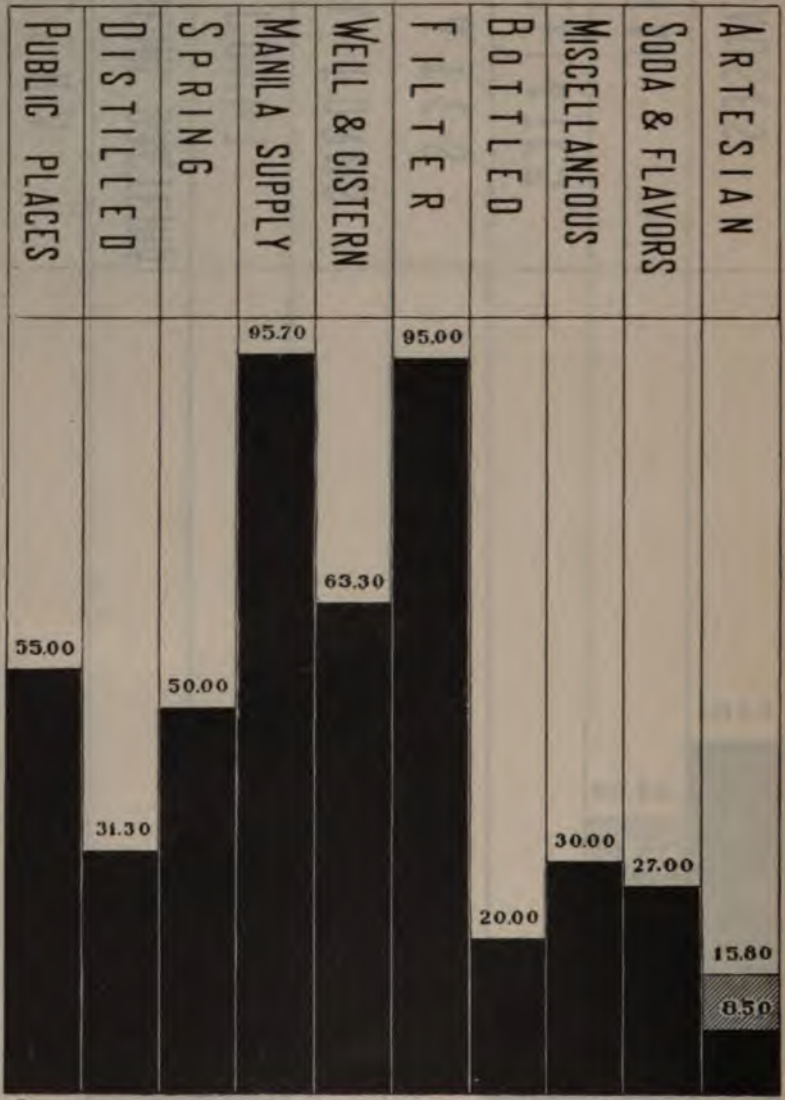
ILLUSTRATIONS.

Charts I and II. 127



PERCENTAGE OF WATER CONDEMNED FOR:

CHART I.



CONDEMNED PERCENTAGE OF WATER OBTAINED FROM

CHART II.

TYPHUS FEVER IN INDO-CHINA.

By A. YERSIN and J. J. VASSAL.[1]
(From the Pasteur Institute of Nhatrang, Annam.)

I.

On May 4, 1906, a thousand or so Tonquin coolies were landed at Nhatrang to serve on the railway in course of construction between Phanrang and Nhatrang. In spite of their youth they were men who had suffered, and they brought with them the poverty and the disease of their country. They were therefore predisposed to catch local endemics, especially malaria, but at the same time they showed affections which are perhaps limited to Tonquin and which in any case have not yet penetrated into South Annam. That recurrent fever came in this way, has already been made known by one of us; typhus fever will now receive our attention.

Our observations are not numerous, and if we have delayed their publication it is because we hoped to supplement them with new ones, but the Tonquinese handicraftsmen have disappeared from our district, and with them the means of pursuing a study which now could be undertaken again more easily in Tonquin.

Nevertheless, our experimental investigations throw new light on the pathogeny of typhus fever and leave no doubt as to the diagnosis of the cases observed in Nhatrang. If writers have dwelt at length on the distribution of typhus fever in Europe, records of its extension in Asia are brief. It exists in Persia, China, and Japan (Netter), but it seems to have attracted but little attention in India. It has never before been noted in the French possessions in Indo-China.

II.

We have been able to follow out seven observations on seven Tonquinese working on the embankment at Hoatan Suoi-Giau, young men between 18 and 20 years old, coming from the Provinces Ninh-Binh, Nam-Dinh. and Ha-nam. Transported under bad sanitary conditions in a crowded and badly organized boat, they were at once obliged to give themselves up to hard and unfamiliar labor in surroundings to which they were not accustomed.

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[1] **Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, February 28, 1908.**

All the cases were observed a short time after their arrival, between May 25 and June 1. The disease disappeared on the spot, without spreading to the native population or the other coolies on the railway. Our observations included five cases of natural and two cases of experimental disease. We will review them briefly.

NATURAL INFECTION.

CASE I.—Hoan Hiet, 20 years of age, from the village of Coi-Tri (Province of Ninh-Binh, south Tonquin), entered the hospital on May 25, 1906, for sores on the legs. On June 1 his temperature rose to 38° C., on the 5th to 40° C. A large abscess was discovered at this time, which was immediately opened. The temperature fell, but rose abruptly twenty-four hours later; after a careful examination it was easy to see that it was not caused by the wound, but that a new affection had begun. Moreover, the sores healed very rapidly. A number of very peculiar symptoms appeared little by little with the pyrexia. The patient fell into a state of profound prostration, which was not stupor but rather a complete annihilation of his strength, accompanied by a nervous upset. He was at times indifferent and dejected, at others delirious and agitated, his attitude was not without analogy to that shown by patients with bubonic plague. The patient complained and groaned continually. There was headache and insomnia. On the third day nausea began and the tongue remained coated without becoming dry. Constipation persisted during the entire illness; the abdomen was neither distended nor painful. The cardio-pulmonary apparatus revealed nothing abnormal on percussion or auscultation, although the breathing was accelerated and the pulse often as high as 120. There was no eruption on the skin nor on the mucosa, but the conjuctiva became considerably injected.

On the sixth and ninth days of the illness, the patient seemed more prostrated than ever, but without ceasing to complain; the prognosis became more serious. Suddenly, on the tenth day, a true crisis set in. The fever fell, the appetite returned and cerebral calm was restored. From that moment recovery was certain and continued without complication and with marvelous rapidity.

The temperature chart was high during ten consecutive days, ranging between 38°.2 and 39°.6 C. during the first eight days, and between 37°.9 and 38° C. on the two last ones. There were only three remissions in the morning between 37°.8 C. The defervescence which had been perceptible on the ninth day was sharply accentuated on the tenth.

CASE II.—Ngo Khoat, of the village of Coi-Tri (Province of Ninh-Binh, south Tonquin), from the same village as *Case I*, entered the hospital the same day as the latter.

The man had been found on the railway embankment already in full pyrexia. He was in a state of great weakness, the conjunctivæ very much injected; no eruption, and no intestinal phenomena were observed; he had been taken ill very suddenly five or six days before. In the hospital, the same principal phenomena were observed as in the preceding case. There was nervous disorder, cephalagia, delirium succeeded by prostration, habitual insomnia and tremor. The fever fell by crisis on the sixth day of his hospital treatment, which was probably the eleventh or twelfth day of his illness. There was a very rapid improvement and recovery without complications.

In spite of careful observation we did not find the least sign of eruption. Both Cases I and II received quinine in large doses by mouth and subcutaneous injection without result. The analysis of the blood, moreover, showed no signs of specific hæmatozoa.

Case III.—Pham Khang, 28 years of age, also from the village of Coi-Tri, was ill several days on the railway works. We witnessed in the hospital only the terminal crisis which developed with remarkable suddenness. From the inquiry we made among the comrades of Pham Khang, we elicited the information that the following symptoms had been noted: Bloodshot eyes, prostration, fever without apparent remissions, constipation, rambling and incoherent complaints. The patient left the hospital on June 5, cured. An examination of the blood proved negative.

Case IV.—Lai van Duc, 26 years of age, from the village of Thuong-Huu (Province of Nam-Dinh, south Tonquin), came into hospital on the second or third day of his illness, which had begun on the railway. We observed six consecutive days of very high fever, reaching 39°.9 and 40° C. with two matutinal remissions to 38.°4 and 38° C. The fall was abrupt; a slight ascent was noted the next day to 37°.4, then a descent to a point well below the normal during four days.

The same phenomena were present as in the preceding cases, except that diarrhœa followed several days of great constipation. No spots of any sort were present, but the conjunctivæ were again excessively red and inflamed. Quinine had no effect and there were no hæmatozoa in the blood.

Case V.—Tran Luan, 24 years of age, from the village of Van-Khau (Province of Nam-Dinh, south Tonquin), entered the hospital on June 1, 1906, in the evening. On one of our weekly visits to the railway embankment, we found him very much prostrated and not able to stand alone. We took him into the automobile, but he was unable to remain in a sitting position without help. We learned that he had suffered from a sudden attack of fever the day before. His illness in hospital lasted ten days, the fever remaining high during six days. On the seventh there was a matutinal remission to 37° C. but the same day it again went up to 39°.3 C. in the evening. The next day there was a marked defervescence, and forty-eight hours later a return to normal, however, with a tendency to hypothermia during several consecutive days. Thus this case resembled those of the other patients. The clinical signs were reproduced with remarkable precision.

Let us repeat once more the characteristic features of this case. First, the sudden attack, fever lasting eleven days, great weakness with delirium, the miserable and distressing aspect of the patient, and lastly the rapid recovery after the crisis, and entire absence of relapse or complications.

Quinine medication was inefficacious and all the examinations of the blood were negative.

EXPERIMENTAL INFECTION.

We had tried in vain to reproduce the disease in the laboratory animals, such as rats, guinea pigs, or rabbits, and we thought that it would be of great scientific interest if we could be enlightened as to the transmission of the disease in the quickest possible manner, namely, by experiments on man. The relatively benignity of this cyclic fever justified this procedure. The positive knowledge of the nature of yellow fever and of its prophylaxis only dates from the first experiments on man

(Reed, Carroll, Agramonte and Lazaer, Marchoux, Salimbeni and Simond). With regard to dengue we have profited in the same manner during the last year (Ashburn and Craig).

CASE VI.—Nguyen van Ky, coming from the village of Nam-Dinh, Van-Khau (Province of Nam-Dinh, south Tonquin), was admitted into the native hospital for ulcers on the legs. His general state of health was excellent. Of robust constitution with a normal heart and without any symptoms of morbid diathesis, this man submitted voluntarily to an inoculation, of which the probable results were not unknown to him.

On June 1 Nguyen van Ky was inoculated under the skin of the arm with 0.50 gm. of blood taken from one of the veins of the arm of Tran Luan (Case V), who was in his second day's illness. The blood collected in a syringe, previously sterilized by steam, was immediately injected without the addition of any foreign substance. There was no reaction at the site of the inoculation. The lymphatic glands of the arm did not show the slightest modification.

The period of incubation lasted fourteen days. Suddenly, without any premonitory symptoms, the patient was seized with an intense fever which persisted for eleven days with slight variations, giving a most characteristic chart, identical in character with the ones taken from the natural illness. The temperature passed in one night from 35°.7 to 39°.5 C. The symptoms of the natural disease were reproduced with the greatest clearness and in addition congestion of the lungs was noted. The excessive prostration of the patient, his wandering thoughts, his insomnia, anorrhexia, coated tongue, constipation, the absence of intestinal phenomena, the suddenness of the attack and the rapid recovery after the crisis, were presented in detail. There was neither eruption nor spots on the skin, but the conjunctivæ were as usual congested.

As in the other cases, our microscopic researches were negative, and no specific febrifuge medication was successful.

CASE VII.—Tran Minh, 21 years of age, from the village of Do Le (Province of Ha-Nam, south Tonquin), entered the hospital on May 28, 1906, for fever and itch. His blood contained *Laverania malariæ*, and he had a series of irregular paroxysms which were checked by quinine. On the twentieth day in the hospital, when our patient had entirely recovered from his attacks of fever and when his blood contained no more hæmatozoa, we proposed to him that he should be inoculated with the blood of a typhus patient, at the time warning him of the probable consequences.

On June 20 he was inoculated under the skin of the arm with the blood of Nguyen van Ky (Case VI), who was in the fifth day of his experimental disease. The technique followed was the same as it was in the first instance. The amount of blood injected was 0.50 gm. and it was absolutely pure. The incubation period upon this second passage was longer than it was with the first patient, it being twenty-one days instead of fourteen. There was no local reaction.

As is seen from the chart, the temperature rose abruptly and remained at a high level for twelve days. It was impossible not to recognize the almost mathematically exact repetition not only of the fever, but of all the other symptoms. We again observed the identical signs; i. e., the abrupt beginning and end, the great weakness, the plague-like delirium, the constipation, insomnia, absence of eruption, blood-shot conjuctivæ, the inefficacy of quinine, and the absence of blood parasites.

III.

The diagnosis of the cases which have been cited was not immediately apparent. We had already observed some cases of spirillar fever among our Tonquinese patients, and therefore we thought ourselves justified in the supposition that we were again dealing with spirillar fever, presenting modified symptoms in the natives of south Annam. However, we hesitated to attribute a new disease, which had never previously been noticed, to the spirilla. The evidence soon became so positive that we were induced to think of typhus fever.

It is true, the eruption was wanting, and we tried in vain to obtain it in the experimental disease. Although failing in this, we succeeded in reproducing a peculiar, cyclic fever, a well-defined disease which corresponded exactly with the description of typhus fever. Although the actual exanthem failed in our cases, it is reasonable to suppose that the congested condition of the conjunctivæ was in a way a substitute.

This is the first time this disease has been described among the Annamese. Is it not possible that it has previously escaped observation because of the absence of an eruption? We know that in sporadic cases and in light ones the eruption generally fails. There have been epidemics without eruption (Dieulafoy), and all writers are agreed in pointing out cases without eruption in the most marked epidemics. Netter observes that "the eruptions in typhus fever are not constant; their absence is noted in a tenth or twentieth of all cases. These facts are not uncommon in the history of eruptive fevers. Dengue, for instance, causes epidemics where eruptions do not appear.

A diagnosis might also be made by elimination, after having reviewed the diseases which resemble typhus fever most closely.

The absence of Laveran's hæmatozoa from the peripheral blood and the spleen, the complete inefficacy of quinine, and the characteristic of the chart, permit us to set aside malaria.

The points of comparison with typhoid fever are very vague, but the differences are sharply accentuated. It is true that the tongue was coated, but it had not the dry and "roasted" appearance of that of typhoid fever; neither were there any intestinal phenomena, but on the contrary constipation. The abrupt start, the course of the chart and the crisis, differentiate our cases from typhoid or paratyphoid fevers.

Spirillar fever would not have passed unperceived at Nhatrang, where it had just been studied for the first time in Indo-China. This fever gives a chart with oscillations and relapses very different from that presented by the disease under discussion; besides, an examination of the blood settles the question.

Kala-Azar is too well known to-day to be confused with this disease.

Dengue is a disease that one meets with in Indo-China, sometimes well characterized, sometimes badly defined. But dengue lasts a still shorter time than typhus, and the charts are in no way comparable, any more than are the different symptoms.

Among the "nonclassified tropical fevers" Manson has described one which he calls "double continued fever," but this is removed from consideration in connection with our typhus by its relapsing pyrexia; and if we even regard the first attack only, the charts are in no way comparable.

IV.

Experiments were first tried on laboratory animals. A certain number of rats, guinea pigs, and rabbits received subcutaneously one or several inoculations of blood taken from patients at different periods of the disease. They manifested neither pathologic phenomena nor elevation of temperature. We have already related our experiments on man.*

The examinations of the circulating blood as well as of specimens taken by splenic puncture, which were very numerous, were always negative.

These results agree entirely with those of Galesesco and Stalineano, in the typhus epidemic of Bucharest in 1906. Besides, we verified the fact as did these authors, that the terminal crisis is accompanied by a very marked and almost pathonomonic increase of mononuclear leucocytes. E. Gotschlich, on the contrary, has described protozoa resembling *P. bigeminum* in typhus patients at Alexandria, which he has called "apiosoma."

Our experiments prove that typhus fever is a disease in which the virus is situated in the circulating blood during the second and fifth days of infection.

It is inoculable from man to man, but does not seem to affect the ordinary laboratory animals. It is possible to make at least two passages on man, but it must be remarked that the incubation is longer the second time than the first (fourteen and twenty-one days).

The specific agent of typhus fever is invisible in the blood or at any rate is exceedingly rare.

These experiments, which doubtless require confirmation and elaboration, authorize us in considering typhus fever as a disease to be classed with the blood infections transmitted by the bites of insects. The transmitting agent has yet to be discovered. Medical literature on typhus, so rich in all kinds of epidemiologic documents, does not disprove this hypothesis.

V.

The therapeutic treatment ordinarily employed for malaria fails in typhus fever. Quinine particularly is useless. We limited ourselves to symptomatic medication.

The origin of our little localized epidemic must either be from the villages of our coolies or the boat which carried them. The infection may be developed later, but the germs seem to come from the south of Tonquin. The first three cases belonged to the same village, Coi Tri (Ninh Binh), and the other two to a bordering province, Nam Binh. The boat need not be considered, for if the disease had originated in it, the number of typhus cases would not have been so limited and there would certainly have been a focus on board, which could not have remained long unnoticed. Moreover, it was a Tonquinese vessel, the home port of which was Haiphong. Inquiry which will be made in the incriminated Tonquinese provinces will soon make it certain whether typhus fever has taken root in Tonquin, and whether new sanitary supervision will not be justified.

CONCLUSION.

1. Typhus fever has been observed in Annam in natives who recently arrived from Tonquin.
2. It manifested itself in accordance with the classic description, with the exception that the eruption was wanting.
3. The direct inoculation of blood from man to man has reproduced the disease after an incubation period of fourteen and twenty-one days.
4. Typhus fever seems to be a blood disease transmitted to man by bites of insects.

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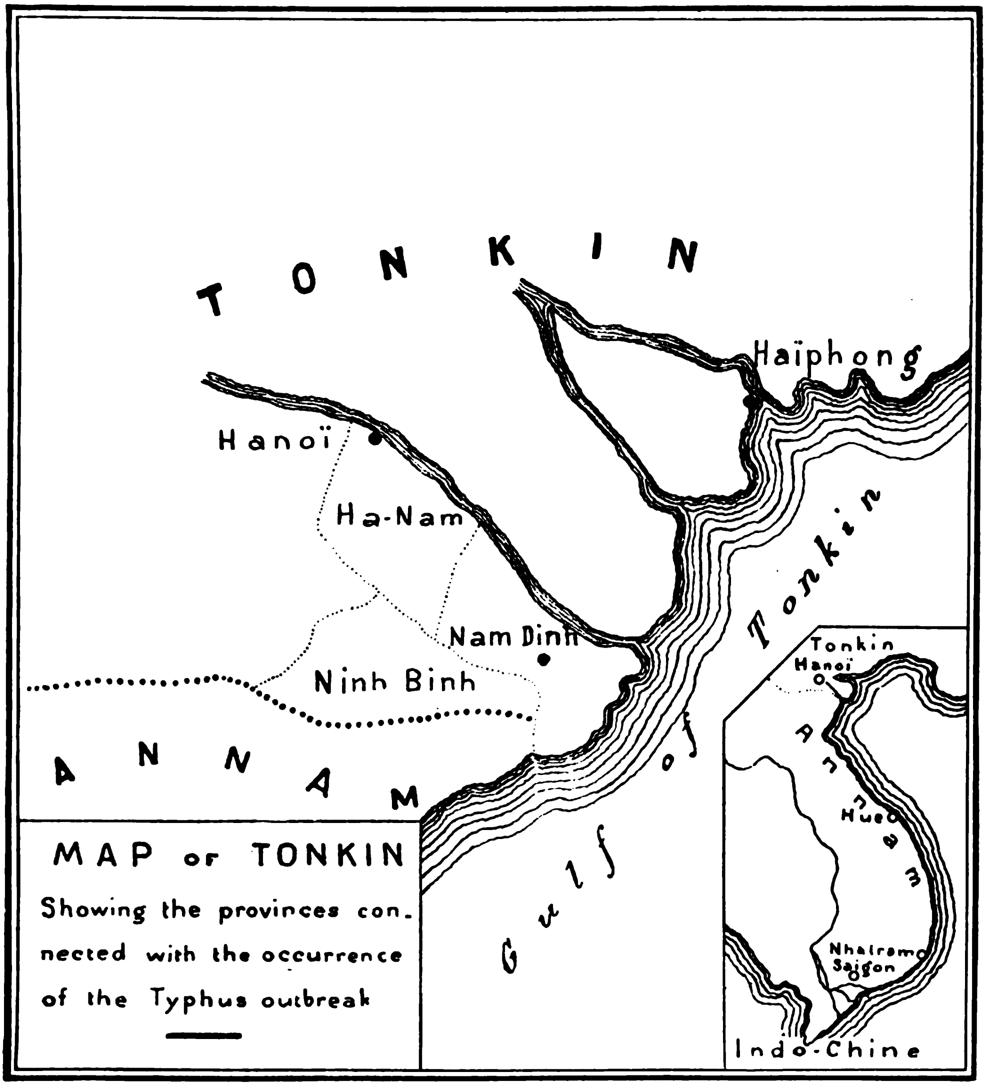
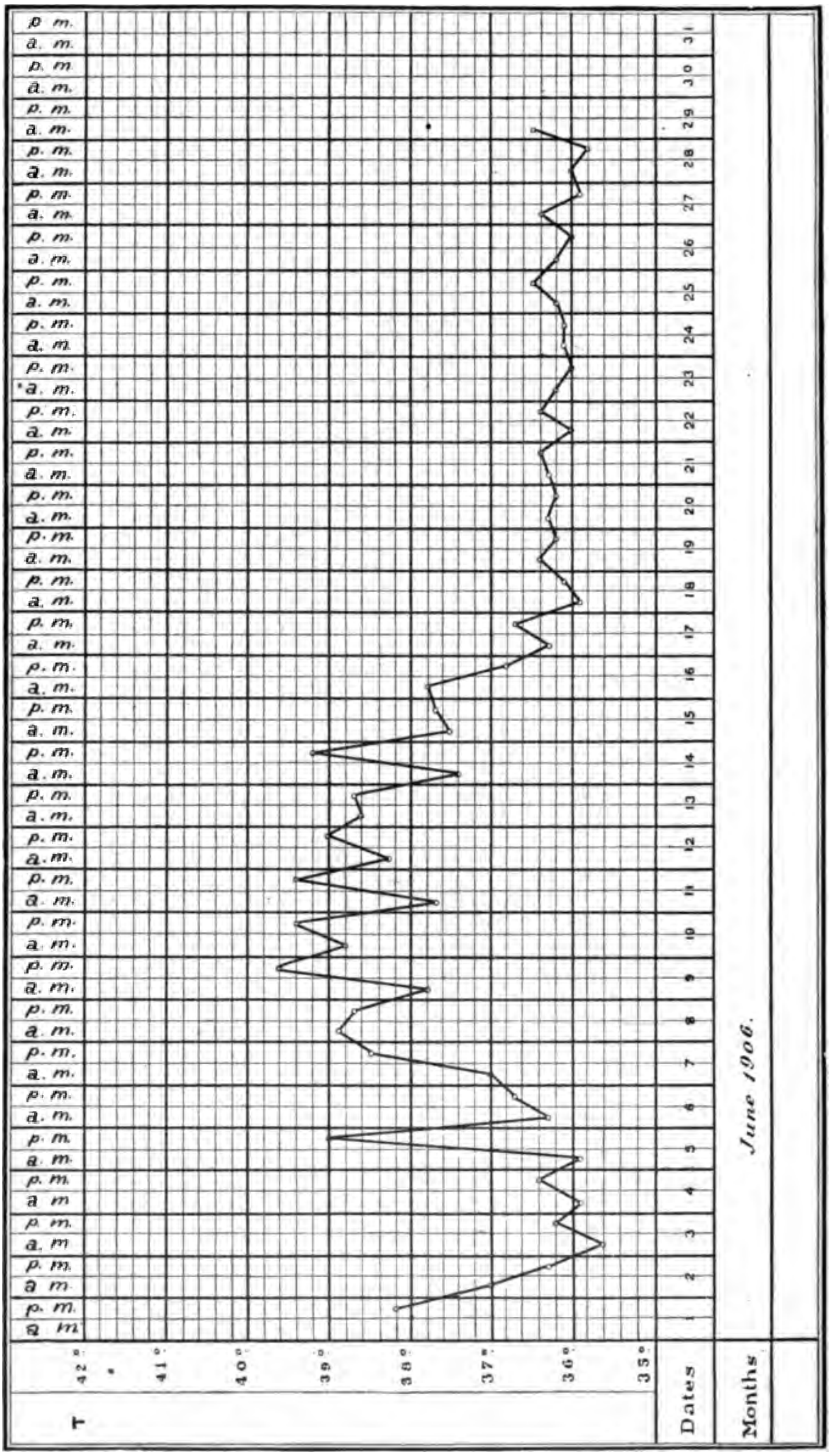
ILLUSTRATIONS.

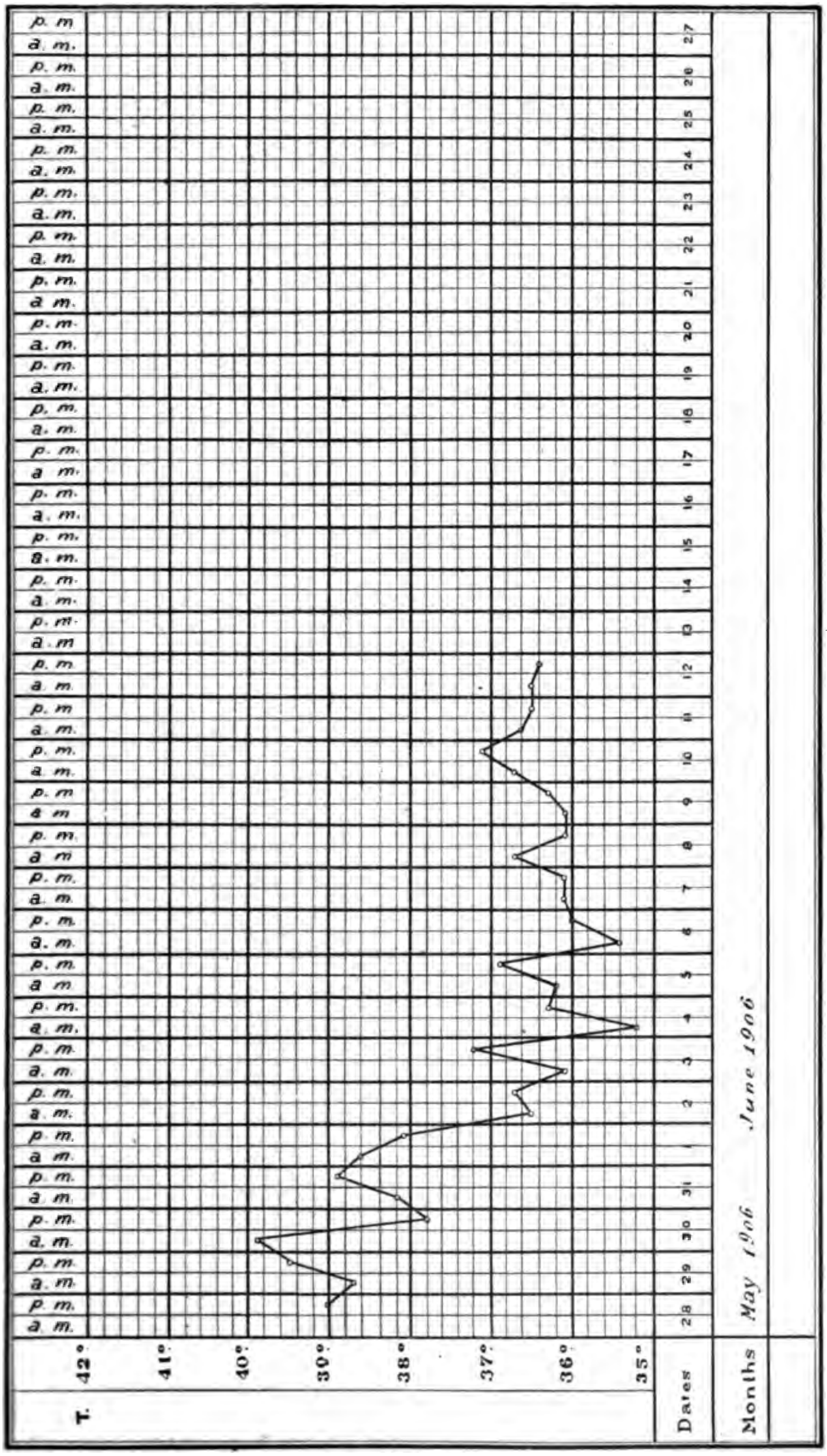
Map of Tonkin and Annam.
Charts 1 to 7.



Map of Tonkin and Annam.



OBSERVATION 1.



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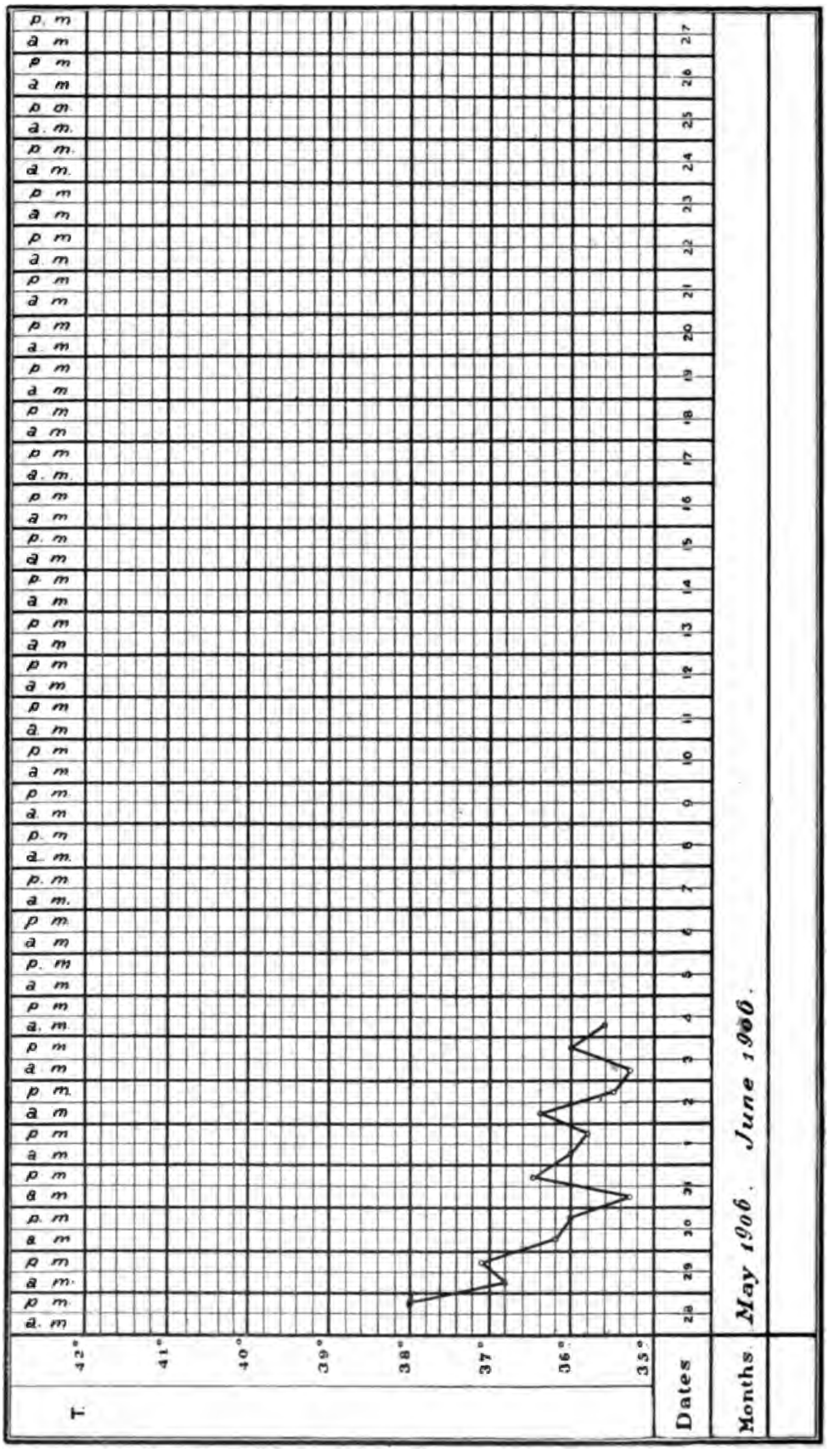

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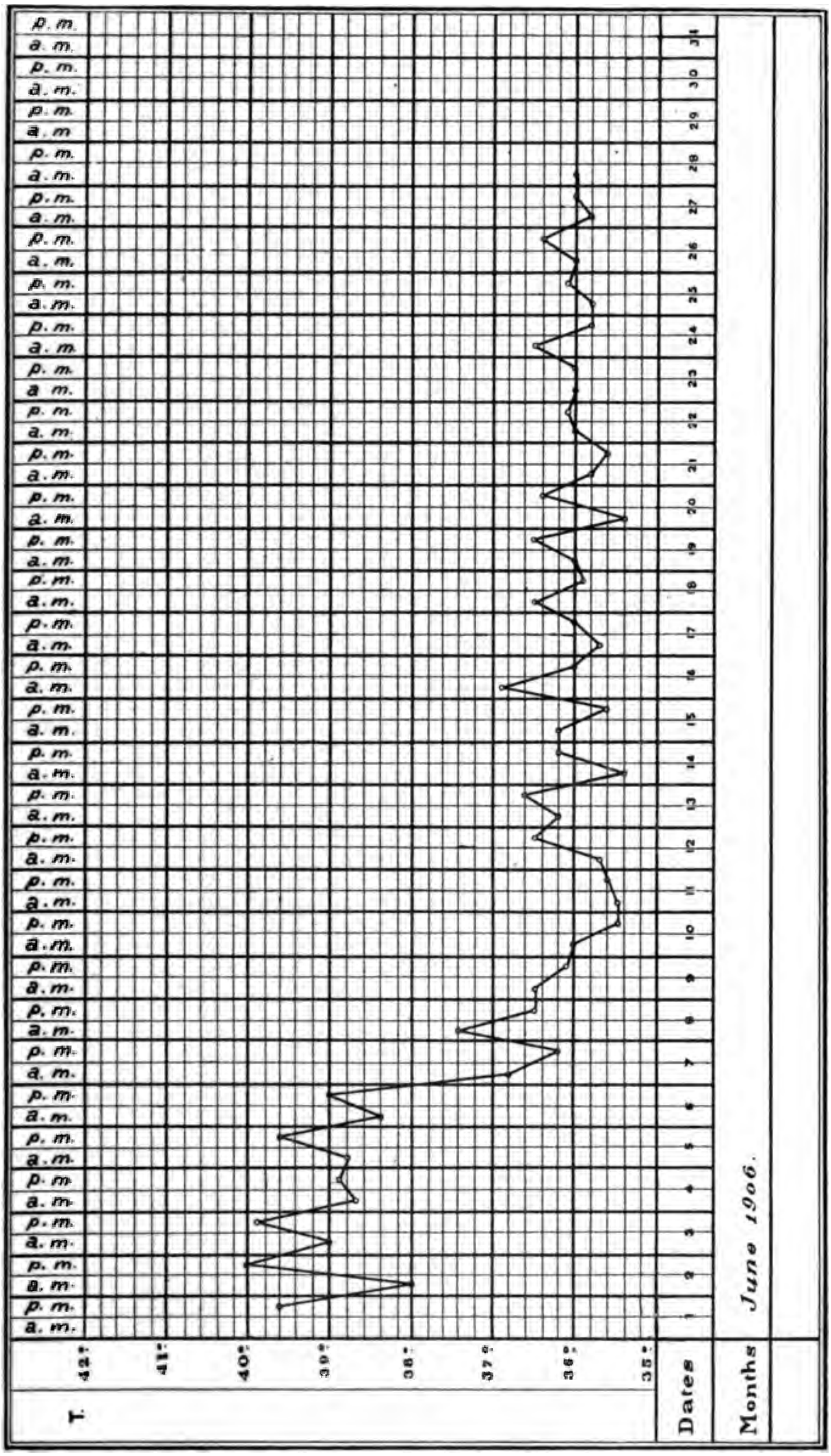

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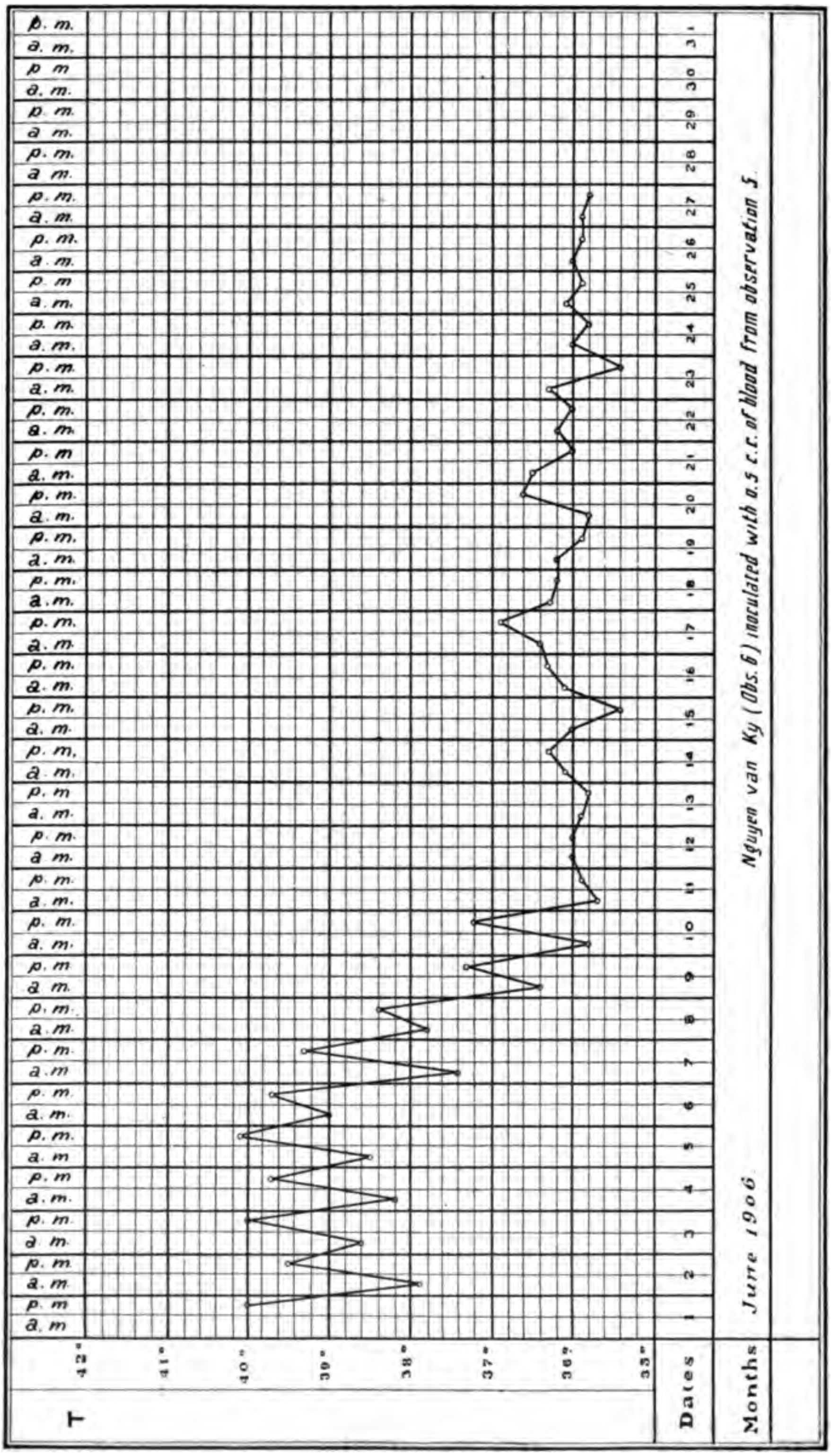
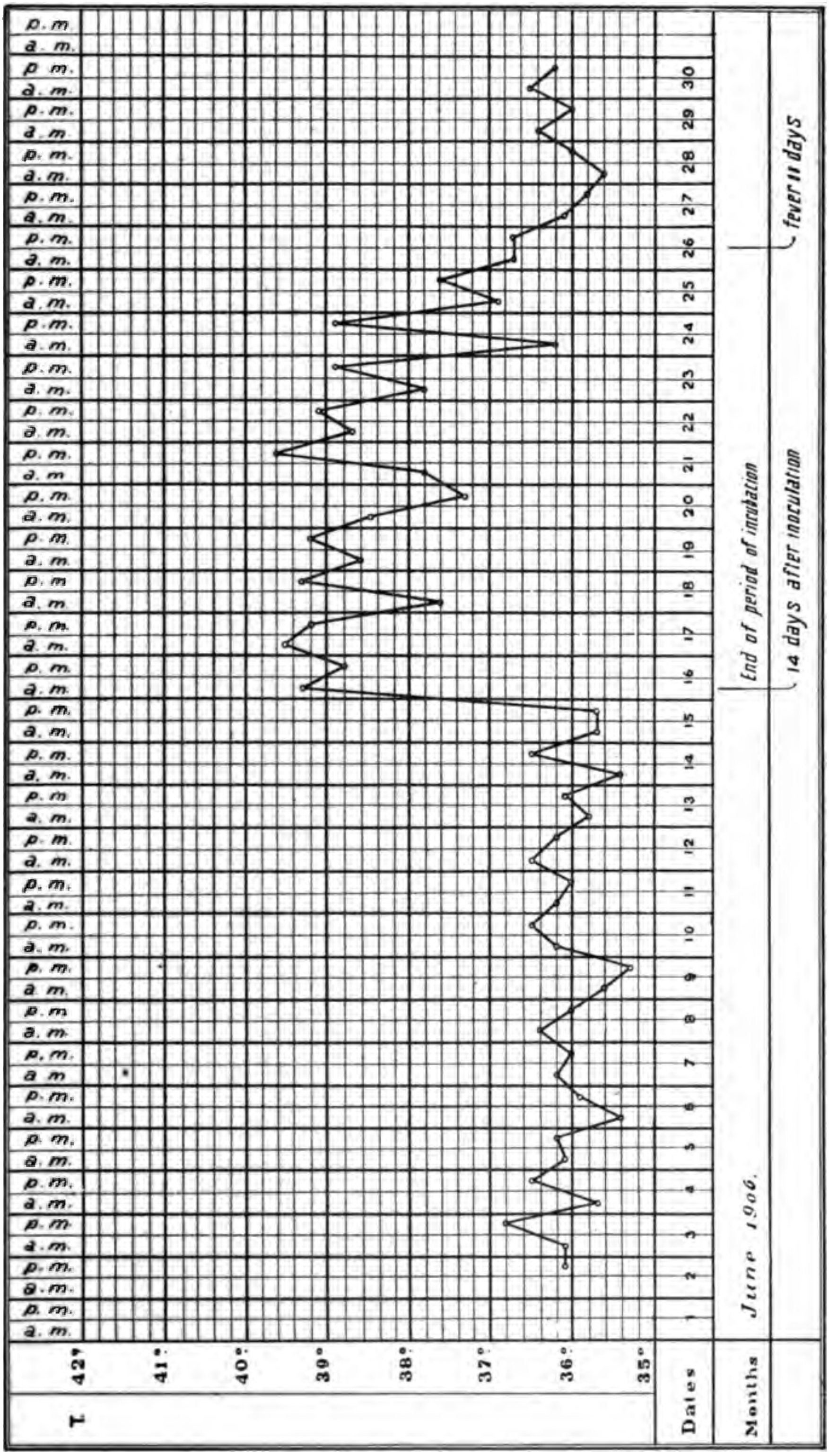
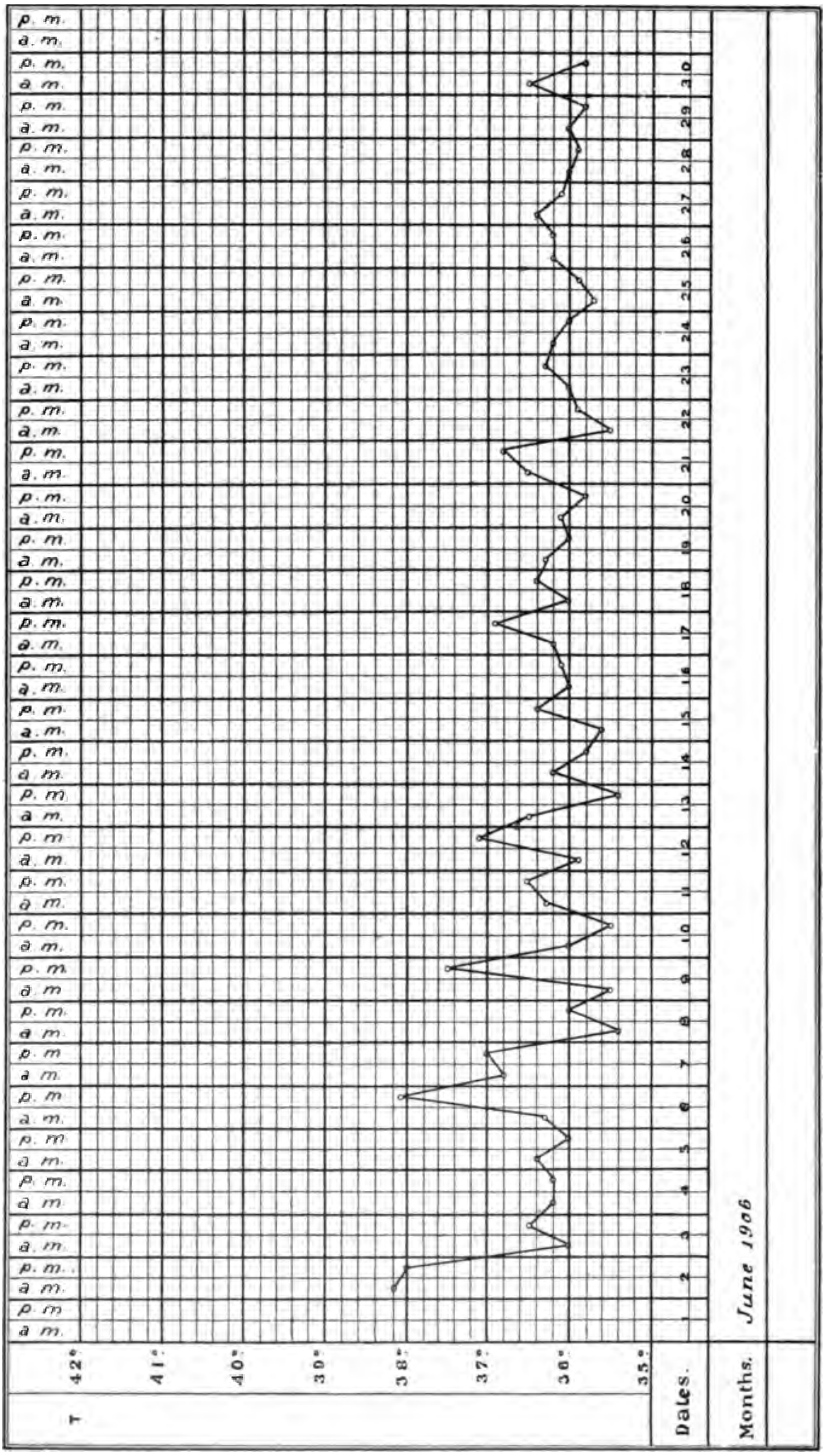


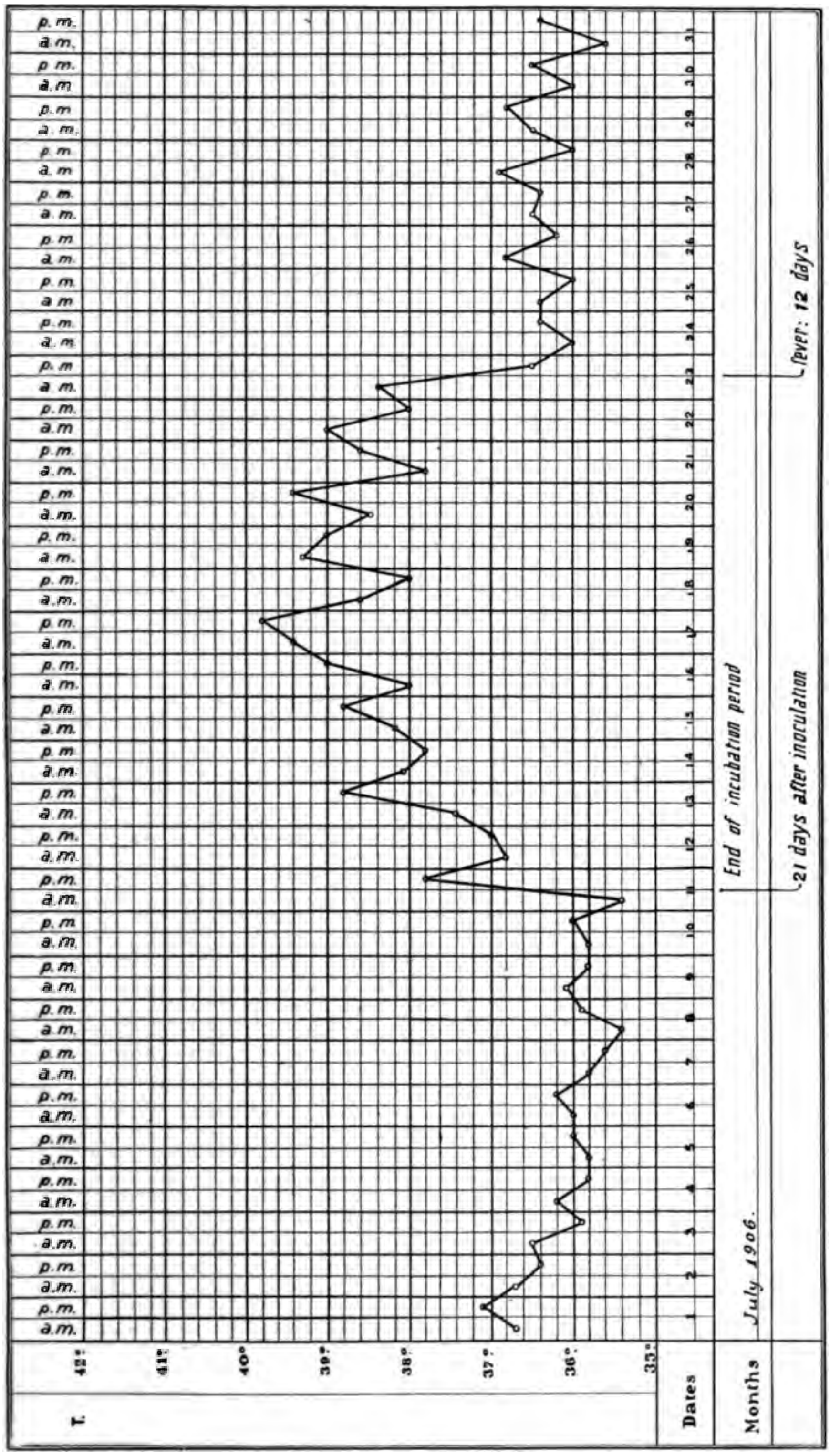
OBSERVATION 5.



Observation 6. June, 1906. Inoculated with 0.5 cc. of blood from Observation 5.



OBSERVATION 7. INOCULATED JUNE 20 WITH 0.5 CC. BLOOD FROM OBSERVATION 6.



OBSERVATION 7—Continued.

ON "HABU" VENOM AND ITS SERUM THERAPY.

By T. Kitajima.[1]
(From the Institute for Infectious Diseases, Tokyo, Japan.)

INTRODUCTION.

Few species of venomous snakes are native to Japan, the main island, Nippon or Hondo, being inhabited only by the relatively harmless *Trigonocephalus Bromhoffi.* But the islands Riukiu (Loo Choo) and Amami (Oshima) are scourged by the fierce snake termed "habu." This species inflicts no little damage upon the population, either killing its victims outright or at least debilitating them seriously. The following table gives the number of cases occurring annually.

Table 1.—*Number of cases bitten by the venomous serpent "habu" from 1898 to 1906.*

Year.	Number of cases.			Recovered.			Deaths.			Infirmities.		
	Men.	Women.	Total.	Men.	Women.	Total.	Men.	Women.	Total.	Men.	Women.	Total.
1898	158	53	211	133	46	179	18	6	24	7	1	8
1899	149	64	213	121	53	174	22	10	32	3	1	4
1900	150	71	221	131	54	185	17	14	31	2	3	5
1901	148	83	231	130	68	198	18	14	32	------	1	1
1902	133	48	181	114	39	153	14	6	20	5	3	8
1903	172	71	243	140	57	197	24	4	28	11	7	18
1904	138	53	191	123	46	169	12	5	17	3	2	5
1905	182	79	261	153	63	216	27	11	38	5	2	7
1906	197	79	276	164	60	224	24	17	41	9	2	11
Total	1,427	601	2,028	1,209	486	1,695	176	87	263	45	22	67

This table shows that 2,028 persons were bitten by this serpent during the past nine years; of this number 263 died, an average of 225 cases with 29 deaths for each year, the death rate being 12.9 per cent. About the same number of cases has been reported from the Riukiu Islands; that is, about 200 a year.

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[1] **Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, February 28, 1908.**

I began the investigation upon which I am now reporting in the year 1902. A branch office of the Institute for Infectious Diseases was established and a temporary laboratory erected at Amami, Oshima, where I could have free access to the habu and so had facilities for collecting the venom. Since the time of beginning the work I have purchased more than 6,000 serpents. Dr. Mine, my former assistant, helped me in various portions of the research, and my present one, Yamamoto, is still engaged in collecting the venom at Oshima. I desire here to express my thanks for their collaboration and for the encouragement given by Professor Kitasato, director of the institute.

THE "HABU" SNAKE.

CROTALINÆ.

Trimeresurus flavoviridis (Hallowell).
Trimeresurus riukiuanus (Hilgendorf).

The length varies from 1 to 1.5 meters; the snake has a large, triangular, flat head which is separated from its spotted body by a distinctly marked neck. The fang is tube shaped. An indentation is present at the back of the eye.

The bites occur during the time from June to December, June and July being most dangerous months. No bitten persons have been reported in January and February. Eighty out of 174 cases were bitten on their lower limbs, 29 on the upper, and a few on the head, face, body, etc. It is dangerous to collect the venom, but finally in the laboratory we encountered a very dexterous manipulator among our employees. Even he would be bitten once or twice a year, but in the end the bites produced only a slight reaction, as he gradually acquired an immunity against the venom.

The process of collecting venom adopted by us is as follows: One of the snakes is taken out of the cage, its head quickly fixed with a forked stick, and as soon as the serpent stretches out its body on the floor its neck is caught with one hand and its mouth opened sufficiently to admit a watch glass, upon which the poison is discharged by compression from outside the sack at position of the poison gland. In our experiments the poison collected from a number of snakes was used for work.

HABU VENOM.

THE PHYSICAL AND CHEMICAL CONSTITUTION OF THE VENOM.

Venom collected from the habu is a viscous, slightly yellowish fluid with an acid reaction, 0.6 cubic centimeter of a 0.01 normal alkali solution being needed to neutralize 1 cubic centimeter. The quantity discharged at one time varies both with the size of the snake and the season of the year; it ranges from 0.5 cubic centimeter to 1 cubic centimeter; in rare cases it is 1.4. When the venom is centrifugated and the supernatant fluid desiccated, it forms a brilliant yellow powder. The amount of this fixed constituent is shown in the following table:

TABLE 2.

Locality from which snakes came.	Number of snakes.	Quantity of venom (cubic centimeters).	Dried (grams).	Fixed substance (per cent).	Average quantity of venom for one snake (cubic centimeter).	Average quantity dried (gram).
Tokunoshima	466	71.40	18.41	25.8	0.153	0.0395
Do	556	81.00	20.85	25.7	0.145	0.0375
Amani	195	58.47	16.46	28.2	0.299	0.0844
Do	418	122.10	27.29	22.4	0.292	0.0653

The dried venom is durable and it dissolves in water giving an opalescent solution with a slight precipitate; it is also almost completely soluble in glycerin, it coagulates at 75° C., and is precipitated by alcohol. It presents all the reactions characteristic of proteids, clearly showing Millon's and Vincent's reactions. It turns polarized rays to the left, and shows no lines of absorption in the spectrum.

Its chemical nature is not yet known clearly. The venom may be brought down by any of the reagents which precipitate proteids. About one-third of the original poison in a 1 per cent solution may be precipitated by adding alcohol to 33 per cent, and one-half of the whole amount of the poison present in the original solution from the filtered fluid will be precipitated by increasing the alcohol to 50 per cent. As more alcohol is added, the amount of precipitation increases, but the amount of the latter finally remains constant after the alcohol reaches 75 per cent. The greater part of the venom is precipitated if one-half the quantity of ammonium sulphate necessary to form a saturated solution is added.

RESISTANCE OF THE VENOM TO PHYSICAL AND CHEMICAL INFLUENCES.

The fact that the resistance of snake venom to heat seems to vary according to the species of snake from which it is collected has been ascertained by Mitchell and Reichert, Calmette, Physalix and Bertrand, Flexner and Noguchi, Lamb, and Ishizuka. · Habu venom presents no change even though it is heated for thirty minutes at 60° C. A 1 per cent solution, however, will precipitate a little by being heated for fifteen minutes at 75° C., while its toxicity is reduced to one-tenth of the original. The principle which causes extravasation when the venom is injected is especially weakened, while the hæmolytic and neurotoxic constituents are scarcely affected. It loses nearly all toxicity if heated for thirty minutes at 90° C. The toxicity of the venom is reduced to one-tenth of the original strength by exposure to the direct sunlight during six hours.

Alkali has a far-reaching effect upon the venom, for when an equal volume of a one-tenth normal solution of sodium hydroxide is added, the toxicity falls to one-thirtieth of the original in twenty-four hours, while normal alkali solution completely inhibits the action of the toxin. The venom is also affected by acids. An equal volume of a one-tenth normal solution of sulphuric acid reduces the toxicity to one-fifth and a normal solution to one-tenth of the original strength after twenty-four hours.

The toxic character of the venom is destroyed by incubation for forty-eight hours at 37° C. with 1 per cent pepsin and 0.2 per cent hydrochloric acid; on the other hand there is a marked resistance to trypsin, which reduces the toxicity only one-half after forty-eight hours. Erepsin has been proved to have no influence over habu venom.

Snake venom is but little subject to the various changes affecting the diphtheria or tetanus toxins, it retains its toxicity unchanged for two months if it is dissolved in an 0.8 per cent salt solution to which 0.5 per cent carbolic acid has been added; however, in the end precipitation gradually sets in with a diminution of the toxicity. A solution in 50 per cent glycerin forms a transparent liquid showing no precipitation, and no diminution of toxicity. For this reason I have adopted the solution in 10 per cent glycerin as the standard and this, after dilution, was used in the usual experiments.

THE ACTION OF HABU VENOM UPON ANIMALS.

Habu venom is one of the most powerful poisons, affecting a very wide range of animals. Guinea pigs, rabbits, mice, rats, etc., which are commonly employed in experiments, die from inoculation of only a small quantity of it. However, its toxicity varies with the season during which it has been collected. The doses lethal after subcutaneous injection are as follows: For the mouse, 0.00005 to 0.0003; guinea pig, 0.0001 to 0.001; rabbit, 0.001 to 0.006.

The following figures are obtained according to von Behring's method by expressing the strength of the venom in terms of the body weight of animal killed by one gram of venom:

1 gram = 30,000 + Ms. to 200,000 + Ms.
1 gram = 500,000 + G. P. to 2,500,000 + G. P.
1 gram = 300,000 + R. to 2,000,000 + R.

or

1 gram = the fatal dose for 30,000 to 200,000 grams of mouse.
1 gram = the fatal dose for 500,000 to 2,500,000 grams of guinea pig.
1 gram = the fatal dose for 300,000 to 2,000,000 grams rabbit.

The above figures show the minimum lethal doses, killing rabbits and guinea pigs in twenty-four to thirty-six hours, and mice in less than twenty-four hours. If the death of the experimental animal takes more time than these fixed hours, it can hardly be relied upon; moreover, the suceptibility of the animal to the snake venom varies greatly in individuals, which makes the experiment more difficult than with the diphtheria toxin.

The differences in susceptibility of different species of animals to this poison is not so marked as it is to tetanus or diphtheria toxin.

The following table shows this, mice being taken as the standard:

TABLE 3.

1 fatal dose per gram of mouse=
 12 fatal doses per gram of guinea pig.
 10 fatal doses per gram of rabbit.
 10 fatal doses per gram of pigeon.
 5 fatal doses per gram of chicken.
 1 fatal doses per gram of dog.
 2 fatal doses per gram of rat.
 ⅙ fatal dose per gram of cat.
 ⅛ fatal dose per gram of frog.

It is evident from the above that the guinea pig and rabbit have the highest susceptibility, while frogs and cats have the lowest.

EXPERIMENTAL.

Mice.—The animals received 0.001 cubic centimeter of venom subcutaneously. The individuals appear ill after five minutes, with erection of the hair; slow, irregular respiration with inspiratory effort; paralysis of extremities causing difficult walking; a tumor is produced at the site of the injection, presenting a dark purple color. The tips of the ears, nose and claws become cyanotic; respiration at length becomes fainter and fainter, the pulse diminishes and is stopped in about forty-five minutes, when death takes place. Convulsions seldom appear.

Post-mortem examinations show a subcutaneous œdema with clots about the site of the injections. The liver, spleen and lungs are anæmic, their size being normal. If the dose used was sublethal, the animal gradually recovers from the affection, while the œdematous areas become necrotic and finally a spontaneous cure is effected at this site.

Guinea pigs.—The animals die in two hours after receiving 0.01 cubic centimeter subcutaneously; symptoms appear in fifteen minutes, swelling is evident at the site of the injection, it turns to a dark, purple color, spreading gradually; the abdomen becomes distended; the animal can not arise to its feet after being turned on its back; respiration becomes slow; the tips of the ears appear pale; shivering sets in, accompanied by a slight opisthotonus. Death takes place after paralysis has developed.

Post-mortem examination shows a subcutaneous œdema with hæmorrhage. The internal organs are anæmic without any other changes. The bowel contents are fluid.

Rabbits.—The animals die in five hours after receiving 0.03 cubic centimeter subcutaneously, practically with the same symptoms as are observed in other animals. A well-developed œdema at the site of injection makes its appearance, accompanied by hæmorrhage. The animal becomes so lethargic that it walks with difficulty and finally can not stand on its feet. An excessive dose, say of 0.04 cubic centimeter, when given intravenously, will kill a rabbit in three to ten minutes. The animal thus treated appears as if in severe pain, and dies after a period of irregular respiration, without any marked changes being observed upon post-mortem examination. If a dose which would kill a rabbit in an interval at some time between thirty minutes and several hours is given intravenously, symptoms identical with the ones which appear after subcutaneous injection are evident, and post-mortem examination shows clots in the pericardium, endocardium and in the mucous membrane of the stomach. Hæmaturia is seldom present.

Five one-hundredths of 1 per cent of the dose which is lethal in subcutaneous injections brings death to the animal when it is injected into the brain. In the latter event perturbation, agitation and convulsions occur and death is preceded by gasping. On post-mortem examination, clots are found at the site of the injection.

Intraperitoneal injection develops the same symptoms as the subcutaneous ones, the only difference being in the severe hyperæmia and ecchymosis of the bowel and other abdominal organs.

In the majority of instances the experimental animals recover gradually when the dose is sublethal. Only now and then death occurs secondarily accompanied by emaciation and conjunctivitis. Other animals die from septicæmia contracted by secondary infection through the ulceraton of the skin.

SYMPTOMS OF HABU POISONING IN MAN.

The region of the bite is of a dark, purple color and shows great swelling, accompanied by a severe burning pain, the latter being characteristic of habu venom intoxication. The lymph glands near the bite also become enlarged and sensitive to pressure. Loss of appetite and vomiting with colic and trouble in the thorax occur in chronic cases, the face is pale; the pulse feeble and rapid (90 to 120). In most instances respiration remains normal. A slight fever is not infrequent. The pupils are neither dilated nor contracted. A cold sweat ending in death finally sets in. The end is also preceded by coldness of the extremities and dyspnœa. Blood in the urine or in the fæces has been observed. Sensory or motor disturbances, which persists after recovery from acute symptoms, are usually due to secondary infections or improper treatment.

HÆMOLYSIS.

Habu venom consists of hæmorrhagic, neurotoxic and hæmolytic. constituents. The hæmolytic action of various kinds of snake venom was observed by M. C. Martin in Sydney, by Calmette, Cunningham and others. Flexner and Noguchi,[2] Kyes,[3] and Ishizuka[4] have each published thorough investigations on the subject. They agree in respect to the complexity of the hæmolytic action of snake venom and find that this action is produced by the coöperation of complements and amboceptors. Kyes discovered that lecithin can act as complement in the hæmolysis produced by venom. The hæmolytic action varies with the different species of animals; our method of studying this phenomenon being as follows:

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[2] *J. Exp. Med.* (1902), **6**, 277.

[3] *Berl. Klin. Wchnsch.* (1902), **39**, 886, 918.; *ibid.* (1903), **40**, 21, 57, 982.

[4] *Ztschr. f. exp. Path. u. Ther.* Heft 1, 4.

A certain amount of venom is mixed with a 5 per cent suspension of the defibrinated blood prepared with 0.8 to 0.9 per cent saline solution, and allowed to stand in an incubator for two hours. After this time it is left at the laboratory temperature for forty-eight hours longer, after which period the result is noted. The action at times would set in very slowly—occasionally not for two or three days. Of course, a control is to be made to distinguish the hæmolysis caused by the venom from the natural laking of the blood. The solution of venom must be prepared immediately before the experiment.

The following table shows the variation of the hæmolytic action with different species of animals:

TABLE 4.

One cubic centimeter of a 5 per cent suspension of blood cells from different animals shows minimal trace of hæmolysis with the following doses:

Dog	0.0000001
Cat	0.0000005
Horse	0.000001
Pig	0.000001
Hen	0.000001
Pigeon	0.000001
Guinea pig	0.00001
Rabbit	0.001
Man	0.0001

The quantities given in the above table are the minimum doses producing hæmolytic action, but five or ten times these amounts are necessary to secure complete laking. The blood corpuscles of cattle, goats and sheep are not affected.

The modification of the hæmolytic action by serum was studied, the following experimental method being used:

The blood corpuscles of the dog and other animals were washed four to eight times in saline solution, and divided into two parts, one of which was mixed with the serum of the same kind of animal and the other left free. Venom was then added to each series.

The following table shows the amount of venom required to produce hæmolysis with the serum-free corpuscles and with those mixed with serum:

TABLE 5.

Animal.	Without serum.	With serum.
	Gram.	*Gram.*
Dog	0.00001	0.0000001
Guinea pig	0.00002	0.00002
Rabbit	0.0001	0.0001
Horse	0.00005	0.000001
Pig	0.000001	0.000001
Pigeon	0.000001	0.000001
Hen	0.0001	0.00001

These figures make it evident that the presence of serum markedly promotes hæmolysis in the cases of the dog and the horse, has no influence in those of the guinea pig, rabbit, pig, pigeon and hen, while with the latter two birds the mixture of the serum even appears somewhat to retard the action.

Experiments were also undertaken to demonstrate whether the accelerator of hæmolysis offers as little resistance to heat as does complement in general, and for this purpose several portions of dog serum were heated for thirty minutes at 60°, 70°, and 80°C., respectively, and were then added to test tubes of washed dog's corpuscles mixed with varying amounts of venom. The resulting hæmolysis is noted in the following table:

TABLE 6.

Dose of venom (gram).	Serum not heated.	Serum heated to—		
		60° C.	70° C.	80° C.
0.00001	Complete	Complete	Complete	Complete.
0.000001	do	do	do	Do.
0.0000001	Partly	Partly	Partly	Partly.
0.00000001	---	---	---	

The hæmolytic action is therefore not affected by heat, even though the temperature be as high as 70° to 80°C. We conclude from this that the action of the serum is not due to ordinary unstable complement, however it may be produced by the presence of lecithin, as was found by Kyes, with cobra venom.

A series of experiments was also made to determine the maximum temperature which the hæmolysin of habu venom would endure. Tubes of a 1 per cent solution of the venom retained about one-tenth and one-thirtieth of the original power of the hæmolysin after being heated for thirty minutes at 60°C. and 70°C., respectively. When heated for thirty minutes at 80°C. the remaining action was exceedingly slight, but still demonstrable. The hæmolysin was completely destroyed after heating for thirty minutes at 90°C. The result is partially shown in the following table, the experiment being made with the washed blood cells of the dog, both with and without serum:

TABLE 7.

Temperature at which a 1 per cent solution of the venom was heated for 30 minutes.	Dose (dried venom) needed in laking 1 cc. of the washed blood cells of dog.	
	With serum.	Without serum.
	Gram.	*Gram.*
60°	0.0000001	0.0001
70°	0.000002	0.0003
80°	0.00002	0.001
90°		
Not heated	0.0000001	0.00001

Although the hæmolytic action is diminished after the solution has been heated for thirty minutes at 60°C., it is interesting to note that this temperature affects only the venom acting on serum-free corpuscles, and the addition of serum restores the power completely. Therefore, the diminution in strength is of a superficial nature, only in part affecting the constitution of venom. Those specimens which were heated for thirty minutes at 70°C and 80°C. exhibited a similar tendency, although with progressive decrease of power. The venom was wholly destroyed at 90°C., after which treatment it failed to act even in the presence of serum. This phenomenon was shown most clearly when experiments were made with the blood corpuscles of the horse. The following table shows the hæmolysis produced in the blood corpuscles of a horse, with heated and unheated venom, the decimals representing the hæmolytic dose required to dissolve 1 cubic centimeter of a 5 per cent suspension of horse's red blood corpuscles.

TABLE 8.

Venom.	Hæmolytic dose of venom.	
	Without serum.	With serum.
	Gram.	*Gram.*
Heated for 30 minutes at 60° C	0.0003	0.000003
Not heated	0.000005	0.000001

The presence or absence of serum does not influence the action of venom upon the red blood corpuscles of guinea pigs, the strength of the venom gradually disappearing as the temperature is raised.

Lecithin was proved to play an important part on the hæmolytic action of habu venom, just as Kyes has observed it to act as an accelerator with other snake venoms.

Ishizuka also seems to have observed the same fact. The following table gives the results of our experiments with lecithin:

TABLE 9.

Dose of habu venom.	1 cc. of a 5 per cent suspension washed red blood cells of dog—	
	With 0.1 per cent of lecithin.	With no lecithin.
1.0 cc. of a 0.01 per cent solution	Complete hæmolysis	Complete hæmolysis.
0.5 cc. of a 0.01 per cent solution	do	Partial hæmolysis.
0.1 cc. of a 0.01 per cent solution	do	Slight hæmolysis.
0.5 cc. of 0.001 per cent solution	do	No hæmolysis.
0.3 cc. of 0.001 per cent solution	Partial	Do.
0.1 cc. of 0.001 per cent solution	do	Do.
0.7 cc. of 0.0001 per cent solution	do	Do.
0.5 cc. of 0.0001 per cent solution	do	Do.
0.3 cc. of 0.0001 per cent solution	Slight	Do.
0 1 cc. of 0.0001 per cent solution	do	Do.

The laking sets in distinctly and quickly in the presence of lecithin even when such a small quantity of venom as 0.01 part of the minimum dose required to effect hæmolysis is used—this being the lowest limit. The blood corpuscles of the guinea pig require 2×10^{-5} gram of venom to produce hæmolysis if lecithin is not added, while they will lake with 2×10^{-8} gram when 0.01 per cent of lecithin is added; i. e., 0.001 of the minimum dose is sufficient to effect the action. Again, the blood corpuscles of cattle do not hæmolyse with venom alone, but a laking was observed to occur with 1×10^{-7} gram of venom when lecithin was present. In every case, the degree of the hæmolytic action differs with the amount of lecithin used. For example, the blood corpuscles of cattle are not affected with 1×10^{-4} gram of venom even if 0.001 per cent of lecithin is added. The following table shows the hæmolytic dose of venom for 1 cubic centimeter of 5 per cent suspensions of corpuscles from various animals treated in each case with 0.01 per cent of lecithin:

TABLE 10.—*Dose of venom necessary to effect hæmolysis in 1 cubic centimeter of a 5 per cent suspension of washed blood cells + 0.01 per cent lecithin.*

Animal.	Dose.
	Gram.
Dog	0.0000001
Horse	0.0000003
Cattle	0.0000001
Guinea pig	0.0000001
Rabbit	0.000001

The venom heated for thirty minutes at 60° C. will effect a vivid hæmolysis when lecithin is added; that is, hæmolysis will make itself manifest in the blood corpuscles of the rabbit even with 0.0001 gram of the heated venom, whereas 0.003 gram is needed if no lecithin is present. The same holds true of the blood corpuscles of the horse and dog. However, the hæmolytic action with lecithin is less than that with serum. This is another instance of the difference of the action between lecithin and serum.

TABLE 11.—*Minimum doses of venom heated for thirty minutes at 60° C. which were needed to effect hæmolysis in 1 cubic centimeter of a 5 per cent suspension of blood cells.*

Animal.	With 1 cc. of a 0.1 per cent solution of lecithin.	Without lecithin.
	Gram.	*Gram.*
Rabbit	0.0001	0.003
Horse	0.0000003	0.0003
Cattle	0.000005	-----------
Dog	0.00001	0.0001

Kyes and Sachs observed the fact that cholesterin inhibited hæmolysis, especially when lecithin is present. Ishizuka made the same observations with habu venom, but I was unable to verify this fact.

AGGLUTINATION.

Habu venom has an agglutinative constituent in addition to that causing hæmolysis. The agglutinative action of habu venom showed some variations dependent upon the species of animal employed. There is no parallel between hæmolytic and agglutinative action. The following table shows the amounts of venom required to agglutinate 1 cubic centimeter of various species of red blood corpucles:

TABLE 12.—*Venom required to agglutinate 1 cubic centimeter of a 5 per cent suspension of defibrinated blood cospuscles.*

Animal.	Amount.
	Gram.
Cat	0.000001
Rabbit	0.0005
Pig	0.0001
Cattle	0.0001
Guinea pig	0.0001
Dog	0.01
Pigeon	0.01
Horse	Negative.
Goat	-----------

The agglutinin was destroyed by heating the solution for thirty minutes at 70°C., whereas the hæmolytic power was retained.

IMMUNIZATION AND IMMUNIZED SERUM.

Immunization with the venom of the family *Crotalidæ* is as a rule difficult to produce, and so it was found to be with the habu venom. I employed horses, cattle, goats, etc., for this purpose, and found that cattle could be made immune with comparative ease, the horse only with the utmost difficulty, several of the latter falling victims to the experiment. The venom was heated or treated with calcium hypochlorite or iodine trichloride in order to diminish the toxicity before introduction into the animal body, but simple dilution with water was also highly satisfactory. The diluted toxin was injected subcutaneously, intravenous inoculation being dangerous and often rapidly fatal to the animal. In most cases we began the inoculation with 0.00001 cubic centimeter of a 1 per cent solution, which was doubled during the first few injections and then increased by small degrees, till at last the dose reached 500 cubic centimeters. It took two years to effect immunization, for the snake venom tends to develop necroses and consequently the interval between injection must be made much wider than is usual with other toxins.

Calmette employs the following method to determine the efficacy of the serum:

> He first determines the dose of venom, which, when given intravenously, will kill a rabbit in from fifteen to twenty minutes, and this is inoculated intravenously fifteen minutes after the animal receives a certain amount of serum intravenously. If 1 cubic centimeter of the serum were needed to protect a rabbit of 2 kilograms' weight, the serum is said to contain 2,000 immunization units. However, I preferred to test the serum after the method of Erhlich and von Behring, mixing the toxin and serum before inoculation.

In order to determine the protective value of the serum, various amounts of the latter are added to tubes containing a 1 per cent solution of the venom. The mixture is allowed to stand for thirty minutes before inoculation. The dose contains ten times the minimum lethal dose for the animal. For instance, if a mouse is used, 0.05 cubic centimeter of a 1 per cent solution of venom should be injected in order to give the animal 0.0005 gram of venom, for the minimum lethal dose for the mouse is 0.00005 gram. This dose is first mixed with a certain amount of serum and then diluted with water so that the whole volume comes to 0.4 cubic centimeter before it is inoculated. The proportions used are as follows per 15 grams of mouse: 0.05 cubic centimeter of a 1 per cent solution of venom, 0.1 cubic centimeter serum, 0.25 cubic centimeter water.

For practical purposes, 0.5 cubic centimeter of a 1 per cent solution of venom, 1 cubic centimeter of serum and 2.5 cubic centimeters of water are mixed, the mixture is allowed to stand for thirty minutes, and 0.4 cubic centimeter of it is inoculated subcutaneously.

A certain interval of time is necessary to effect a complete neutralization of venom with serum. If the mixture is injected immediately after it is prepared, the free venom will often kill the animal and therefore, in every case it is allowed to stand for thirty minutes. Even then, the results obtained are not perfectly uniform, for occasionally an animal receiving a large quantity of serum dies, while the one which receives less serum survives. This is due to the wide differences in individual susceptibility. Therefore, the standardization of the serum should be repeated over and over again. I employed mice or guinea pigs in the experiment, because the abundant supply of these animals gives facilities for making a wide series of experiments with a great number of animals. Five one-hundredths cubic centimeter of the immune serum prepared by me neutralizes 0.05 cubic centimeter of a 1 per cent solution of venom; that is, a certain quantity of serum neutralizes the same volume of a 1 per cent solution of venom. Sometimes serum with double this power was obtained but it was exceptional. I found that antiserum prepared by Calmette had no effect on habu venom, while ten immunization units of antitetanus serum could neutralize 0.0001 gram of venom. Again, the antihabu serum was observed to have no power over the poison of the common Japanese viper.

THERAPY.

Antihabu serum has been tried upon a number of cases in Amami, Oshima, and Riukiu since 1905. In most cases the serum has been distributed among the practitioners of the islands gratis. They are required to report the result.

A habu discharges, under natural circumstances, 0.3 cubic centimeter to 0.5 cubic centimeter of poison, equaling about 0.1 gram of the dried venom. This dose will be neutralized by 10 cubic centimeter of serum; however, for curative uses, the dose must be increased to a considerable degree, as the venom is usually introduced several hours before the immune serum is injected. At present 40 cubic centimeters of serum are put in a bottle as a curative dose for one case. In a chronic case, twice the dose or more is used. The injection is made near the bite, which is incised slightly, washed and dressed in the usual manner.

One hundred and eighteen patients were treated with serum of whom five died, making a death rate of 4.2 per cent. Further, of these five deaths, one received 40 cubic centimeters of serum after three hours had elapsed after the bite had been received and the patient died in a few minutes after the injection was made. We may safely exclude this case from the above figures and then the death rate becomes as small as 3.4 per cent. Of the remaining four deaths, one case expired of weakness arising from loss of blood, another of pyæmia in six days, while another succumbed in nine days, and the remaining one died in sixteen hours.

Appended is a sample of the reports, which are made upon the printed form packed with each bottle of serum:

Result obtained by the administration of antihabu serum.

Patient:	
Residence	Kanehisa Village in Oshima.
Occupation	Peasant.
Name	Jiro Yamada.
Age	42.
When and where bitten	4 p. m. Dec. 5, 1905; Yaiyama in Kanehisa village.
Site of bite and appearance	At the middle of the right palm. The bite consists of several wounds as if stuck with needles; purplish in color; swelling considerably.
General symptoms	Swelling increased by degrees. Extended as far as the third of the upper limb; burning pain; glands swollen; painful on pressure; temperature, 39; pulse, 110; face pale; vomiting, colic, and restlessness developed.
Prognosis at the first examination	Bad.
Serum:	
First injection—	
Date and hour	7 p. m. Dec. 5, 1905.
Amount	40 cubic centimeters.
Second injection—	
Date and hour	10 p. m. Dec. 5.
Amount	40 cubic centimeters.
Total amount of serum injected	80 cubic centimeters.
Site of injection	
Other treatment if any	Dressed the wound with aseptic treatment; gave emulsion of digitalis.
Duration after injection was made	Amelioration of symptoms developed on the second day after inoculation; on third nearly cured, except necrosis at bite.
Result	Lived.
Remarks	
Physician:	
Name	T. Tamaru.
Address	Naka Kanehisa village in Oshima.

We have come to the following conclusion, drawn from all the reports we have received: The serum has a marked tendency to ameliorate the intoxication, bringing about a quicker recovery. If it is given immediately after the bite, swelling only makes its appearance, with only the slightest phenomena of intoxication. In ordinary cases, general symptoms such as vomiting, colic and pain soon disappear, pain at the site of the bite also decreases in two to three hours and the swelling subsides after serum treatment.

The importance of serum therapy is well shown by the fact that the death rate was reduced to one-third of the ordinary. However, we regret that the ignorance of the people as well as of the physicians of the islands and the difficulties of communication make the poor victims forego serum treatment in the general run of cases. Possibly no death will occur if the victim receives serum treatment within one hour after the bite.

In conclusion, I must acknowledge my indebtedness to Professor Kitasato, director of the Institute for the Study of Infectious Diseases, for promoting these studies.

FILTRATION EXPERIMENTS WITH VIRUS OF CATTLE PLAGUE.

By E. H. Ruediger.

(From the Serum Section of the Biological Laboratory, Bureau of Science.)

INTRODUCTION.

The question as to whether the virulent factor of the blood of animals sick with cattle plague will or will not pass the Berkefeld or Chamberland filter is still an open one, and therefore a legitimate subject for investigation. The following brief review of the literature will make this conclusion clear:

Semmer, in the year 1895[1] reported that the contagium of cattle plague does not pass through the Chamberland filter. No mention is made in the reference whether he used filter F or filter B. Nencki, Sieber and Wyznikiewicz[2] found that extracts made from the organs of an animal suffering from cattle plague transmitted the disease when injected under the skin of nonimmune animals. After having been filtered through either the Berkefeld or the Chamberland candles these extracts were entirely harmless. Kolle and Turner[3] state that cattle-plague blood or bile are rendered nonvirulent on being passed through either the Berkefeld or the Chamberland filter. In order to exclude the possibility of an intracorpuscular microbe which might not be free in the blood, they dissolved the red blood corpuscles by mixing defibrinated blood with 0.2 per cent solution of sodium chloride. Inoculation experiments with filtrates of laked blood gave identical results.

Nicolle and Adil-Bey[4] found that the virus of cattle plague does not pass through the Berkefeld nor through the Chamberland filter, one part of defibrinated blood having been mixed with nine parts of water. In a later report[5] these authors state if peritoneal fluid is used for experimental work the filtrates from the Berkefeld and from the Chamberland filters are frequently infectious. Yersin,[6] on repeating the experiments of Nicolle and Adil-Bey verified their results. He injected physiological salt solution into the peritoneal cavity of an animal sick with cattle plague; four hours later he collected the peritoneal fluid, filtered it and with the filtrate inoculated nonimmune cattle.

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[1] *Deutsche Zeitschr. f Thiermedicin* (1895), **22**, 37.

[2] *Centrbl. f. Bakteriol. Orig.* (1898) **23**, 535.

[3] *Ztschr. f. Hyg. u. Infcktionskrankh.* Leipzig (1898), **29**, 361.

[4] *Ann. d. l'inst. Pasteur* (1899), **13**, 323.

[5] *Ibid.* (1902), **16**, 56.

[6] *Ibid.* (1904), **18**, 429.

The results obtained showed that the virus passed through Chamberland filters marked F but not through those marked B.

Memmo, Martoglio and Adani[7] came to the conclusion that the virus of cattle plague passes through the Berkefeld filter, but is arrested by the Chamberland. These authors experimented with virulent blood diluted with physiologic salt solution and filtered under pressure equal to one-half an atmosphere.

Woolley[8] closes his experiences on filtration as follows: "Apparently to judge from these results the causative agent of the disease may or may not pass through the pores of the Pasteur-Chamberland filter according to the conditions surrounding the experiment." What these conditions are the author fails to mention.

Recently Todd[9] defibrinated virulent blood by whipping, diluted it by adding four times its volume of physiological salt solution (0.8 per cent), and divided it into two parts, part A and part B. Part A he passed through a large, close-pored Berkefeld filter as slowly as possible; part B through a large and very porous one as rapidly as he could. Filtration was carried out by suction from an ordinary laboratory water pump and the difference of pressure was less than one atmosphere.

Fifty cubic centimeters of each of these filtrates injected under the skin of cattle proved to be entirely harmless. Three control animals which were inoculated with one-fifth cubic centimeter of the same blood before it was filtered contracted typical cattle plague. Ten days after the inoculation with the filtrates he injected the same animals with 10 cubic centimeters of virulent blood; they all contracted cattle plague, showing that they were not immune to the disease.

In a second experiment, Todd introduced 40 cubic centimeters of citrated virulent blood into the interior chamber of a sterilized Chamberland filter marked F. After carefully closing the open end of the filter, he placed it in the peritoneal cavity of an animal from Cyprus. It remained well. Thirteen days later he inoculated the animal with virulent blood, it contracted cattle plague and died eight days later.

In closing his report Todd says: "Reviewing the work which has been published on this question and the results of the experiments cited above, one is led to the conclusion that there is insufficient evidence in favor of the active agent of cattle plague being capable of passing through a filter.

It will be seen from the foregoing that there is a wide discrepancy in the results of the different workers. Semmer, Nencki, Sieber and Wyznikiewicz, Kolle and Turner, and Todd agree that the virus of cattle plague will not pass any ordinary germ-proof filter. Memmo, Martoglio and Adani find that it passes through the Berkefeld filter but not through the Chamberland. Nicolle and Adil-Bey, as well as Yersin, state that it passes the Berkefeld and the Chamberland marked F, but is arrested by the Chamberland B. According to Woolley the virus may or may not pass the the pores of the Pasteur-Chamberland filter. Although there are wide discrepancies in the results reached by these authors, the distinctions are perhaps not greater than the differences in the methods employed by them.

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[7] *Ann. d'Ig. Sper.* (1904), **14**, 291.

[8] *This Journal* (1906), **1**, 582.

[9] *J. of Hyg.* (1907), **7**, 570.

In carrying out the experiments to be detailed I made an attempt to repeat the various methods employed by different workers, and am able to report on the following:

I. Filtration of bile. II. Filtration of blood diluted with salt solution. III. Filtration of blood laked with distilled water. IV. Filtration of peritoneal fluid.

Throughout these tests great precautions were taken to prevent accidental infection of the experimental animals. In order fairly well to exclude the possibility of their having been accidentally infected before inoculation, the cattle were kept under observation in a fly-proof stable for at least seven days. If during this time no symptoms manifested themselves the animals were inoculated. Two control animals, A and B, were kept with each experiment. A received unfiltered material, while B remained uninoculated. Animal A was isolated in a fly-proof shed, animal B remained with those that were inoculated with filtrate. Animals that did not contract cattle plague from the filtrate were afterwards tested for immunity with virulent blood. The animals used were from Sibuyan Island as, so far, animals immune to cattle plague have not been encountered among cattle from that point.

EXPERIMENTAL.

No. 1.—The bile was collected and mixed with an equal part of physiological salt solution during the post-mortem examination on an animal bled to death for virulent blood. The mixture was divided into four parts, designated as *a, b, c,* and *d.* Part *a* was not filtered, *b* was passed through a Berkefeld filter V, *c* was filtered through a Berkefeld candle N, and *d* was passed through one marked W.

Four animals, Nos. 1, 2, 3, and 4 were inoculated.

Animal No. 1 received 50 cubic centimeters of part *a* under the skin. On the seventh day after the inoculation the temperature rose and the animal died of cattle plague on the thirteenth day. (See Chart No. 1.)

Animal No. 2 was injected with 50 cubic centimeters of *b.* Cattle plague did not follow. (See Chart No. 2.) Nineteen days later 10 cubic centimeters of virulent blood was given subcutaneously. In four days the animal sickened with cattle plague and was bled to death for virulent blood on the sixth day after inoculation. (See Chart No. 2′.)

Animal No. 3 received 50 cubic centimeters of *c.* It remained well. (See Chart No. 3.) Twenty days later it was inoculated with 10 cubic centimeters of virulent blood; it sickened with cattle plague three days later and was bled to death on the sixth day. (See Chart No. 3′.)

Animal No. 4 inoculated with 50 cubic centimeters of *d,* remained well. (See Chart No. 4.) After sixteen days it received 10 cubic centimeters of virulent blood, it sickened with cattle plague on the fourth day and was bled to death on the tenth after inoculation. (See Chart No. 4′).

No. 2.—Virulent blood was diluted with four times its volume of physiological salt solution and the mixture divided into four parts designated as *a, b, c,* and *d.*

Part *a* was not filtered, *b* was passed through a Berkefeld filter V, *c* was filtered through a Berkefeld candle marked N, and *d* was passed though one marked W.

Four bovines, Nos. 5, 6, 7, and 8 were inoculated with these materials.

Animal No. 5 received 50 cubic centimeters of *a*, it developed cattle plague on the fourth day after inoculation and was bled to death on the tenth. (See Chart No. 5.)

Animal No. 6 was inoculated with 50 cubic centimeters of *b* and remained well. (See Chart No. 6.) Twenty-eight days later the animal received 10 cubic centimeters of virulent blood, it showed symptoms of cattle plague on the third day and was bled to death on the sixth. (See Chart No. 6'.)

Animal No. 7 was injected subcutaneously with 50 cubic centimeters of *c.* No symptoms appeared. (See Chart No. 7.) Seventeen days later it was inoculated with 10 cubic centimeters of virulent blood, it developed cattle plague and was bled to death on the eighth day after inoculation. (See Chart No. 7'.)

Animal No. 8 received 50 cubic centimeters of *d*, it remained well. (See Chart No. 8.) After one month 10 cubic centimeters of virulent blood were injected, the temperature began to rise within twenty-four hours and the animal was found dead on the morning of the sixth day. (See Chart No. 8'.)

No. 3.—One part of virulent blood was laked in four parts of distilled water and the resulting solution was divided into four parts, *a, b, c,* and *d.*

Part *a* remained unfiltered, *b* was passed through a Berkefeld filter V, *c* was filtered through a Berkefeld candle N, and *d* was passed through a Berkefeld filter marked W.

Of four bovines, Nos. 9, 10, 11, and 12, animal No. 9 was inoculated with 50 cubic centimeters of *a.* The animal showed cattle plague on the third day after inoculation and was bled to death on the seventh. (See Chart No. 9.)

Animal No. 10 received 50 cubic centimeters of *b* under the skin. It remained well. (See Chart No. 10.) On the nineteenth day 10 cubic centimeters of virulent blood were injected, this procedure was followed by cattle plague in four days. (See Chart No. 10'.)

Animal No. 11 was inoculated with 50 cubic centimeters of *c.* This proved to be noninfectious. (See Chart No. 11.) Eighteen days later the same animal was inoculated with 10 cubic centimeters of virulent blood, it sickened with cattle plague in two days and was bled to death on the fifth day after inoculation. (See Chart No. 11'.)

Animal No. 12 received 50 cubic centimeters of *d* and remained well. (See chart No. 12.) After twenty days it was injected with 10 cubic centimeters of virulent blood. Cattle plague manifested itself on the fifth day and the animal was bled to death on the eighth. (See Chart No. 12'.)

No. 4.—This experiment is an attempt at repeating the work of Nicolle and Adil-Bey and that of Yersin.

Two liters of sterilized physiological salt solution were injected into the peritoneal cavity of an animal sick with cattle plague. One hour after the injection, the animal was bled to death, the abdomen opened and the peritoneal fluid collected. The collected fluid was diluted with an equal part of physiological salt solution and divided into four parts, *a, b, c,* and *d.* Part *a* was not passed through a filter, part *b* through a Berkefeld candle V, *c* was through a Berkefeld filter marked N, and *d* through one marked W.

Four bovines, Nos. 13, 14, 15 and 16 were inoculated with these fluids.

Animal No. 13 received 50 cubic centimeters of part *a,* it sickened with cattle plague on the third day and was bled to death on the sixth after inoculation. (See Chart No. 13.)

Animal No. 14, inoculated with 50 cubic centimeters of *b,* sickened with cattle plague within three days and was bled to death on the fifth day. (See Chart No. 14.)

Animal No. 15. Fifty cubic centimeters of *c* were injected into animal No. 15. Cattle plague appeared on the sixth day and the animal was bled to death on the tenth after inoculation. (See Chart No. 15.)

Animal No. 16 was inoculated with 50 cubic centimeters of *d,* it developed cattle plague within three days and was bled to death on the eighth. (See Chart No. 16.)

CONCLUSIONS.

According to the reports of other writers and the results above recorded, it appears that the causative agent of cattle plague present in the bile and in the blood of an animal sick with that disease does not pass through the pores of Berkefeld filters marked V, N, or W.

If one injects physiological salt solution into the peritoneal cavity of an animal suffering from cattle plague and collects the fluid one or two hours later, the fluid appears to be infectious after having been passed through either one of these three Berkefeld filters.

These results are somewhat unintelligible and the tests with peritoneal fluid will need to be repeated a number of times before accidental infections from other causes can rigidly be excluded.

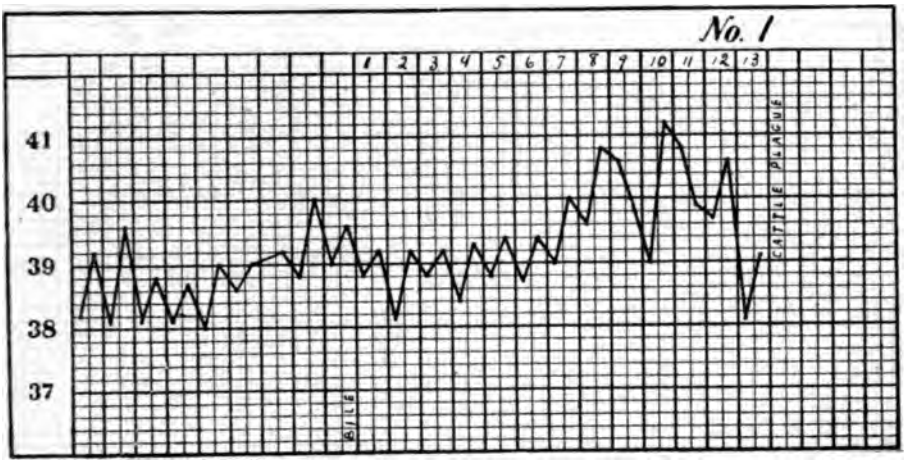
Peritoneal fluid, prepared as above described, appears to be fully as virulent as the blood of the animal. Two serum animals are now being immunized with this fluid, the value of their serum will be compared with that of animals immunized with virulent blood, and the results reported in the near future.

ILLUSTRATIONS.

Charts 1 to 16 and 2′ to 11′.

ILLUSTRATIONS.

Charts 1 to 16 and 2′ to 11′.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BILE
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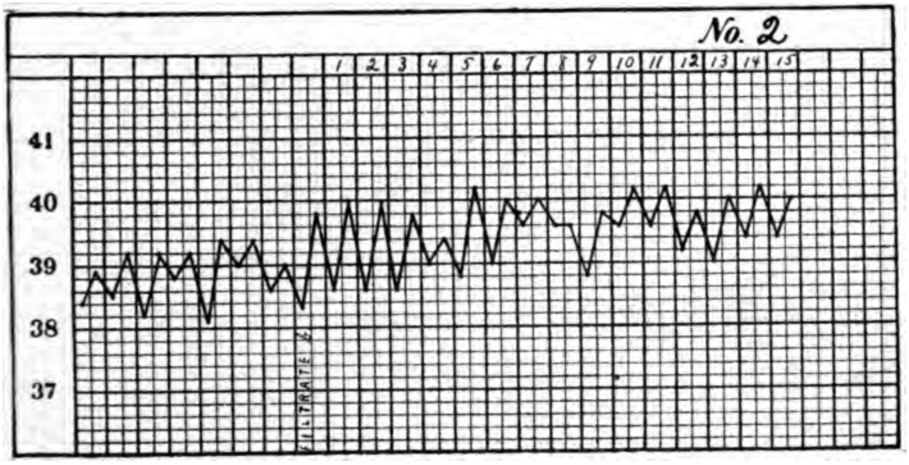
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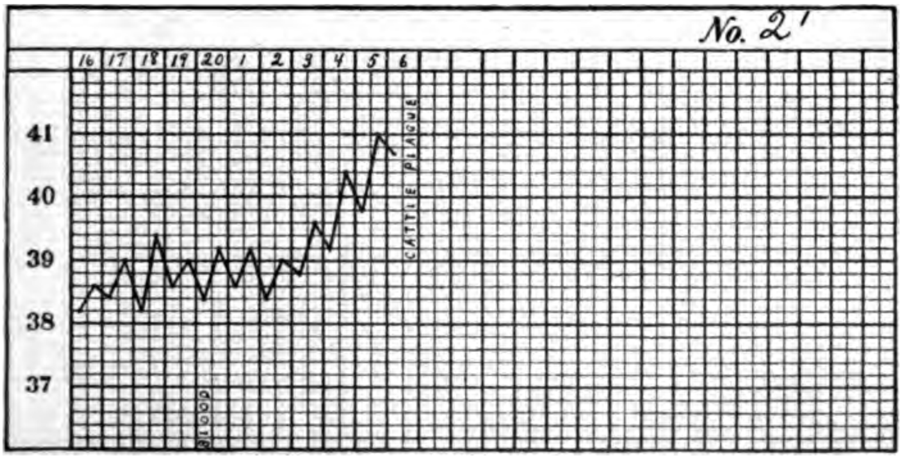
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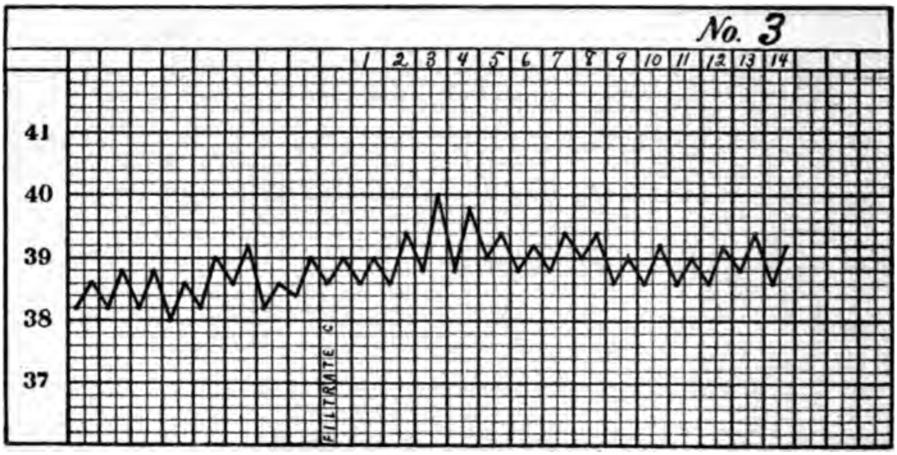
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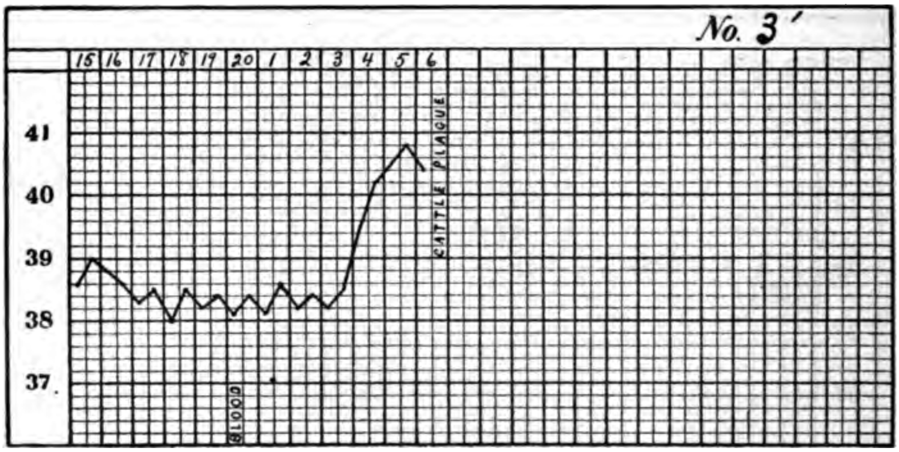
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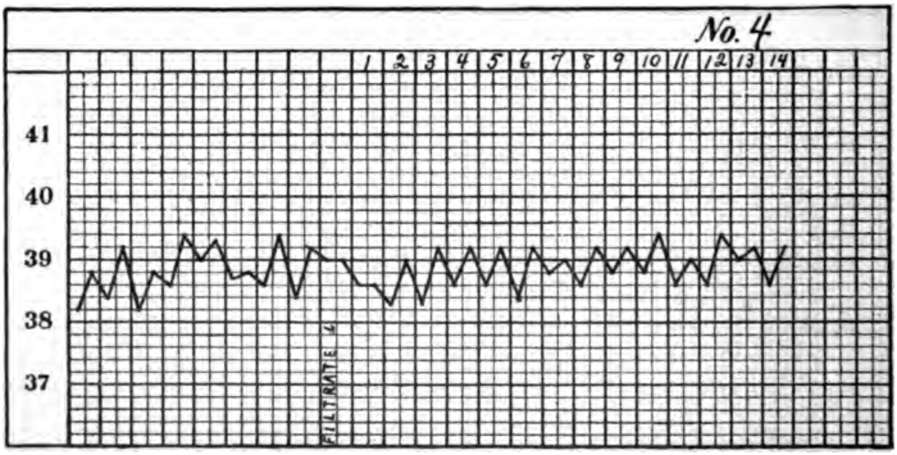
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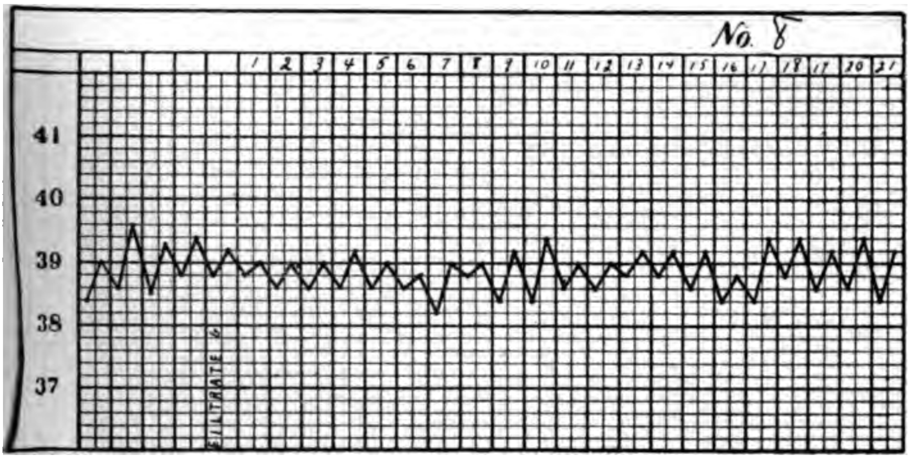
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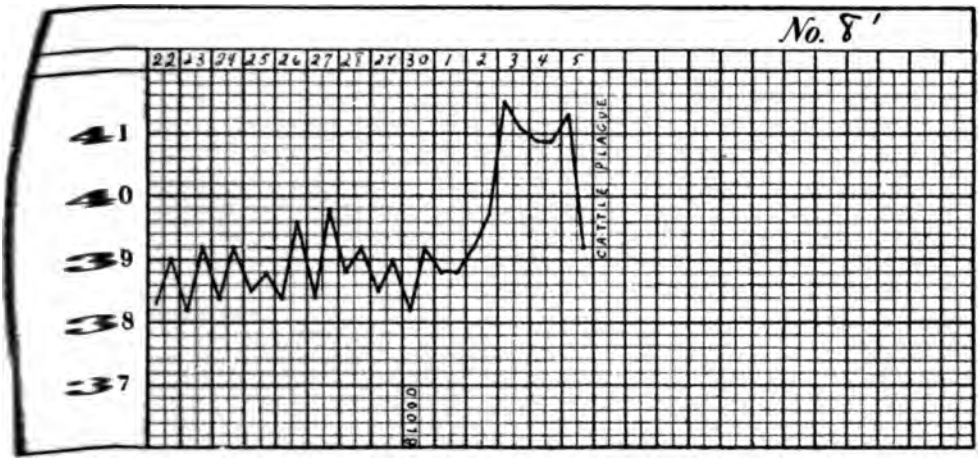
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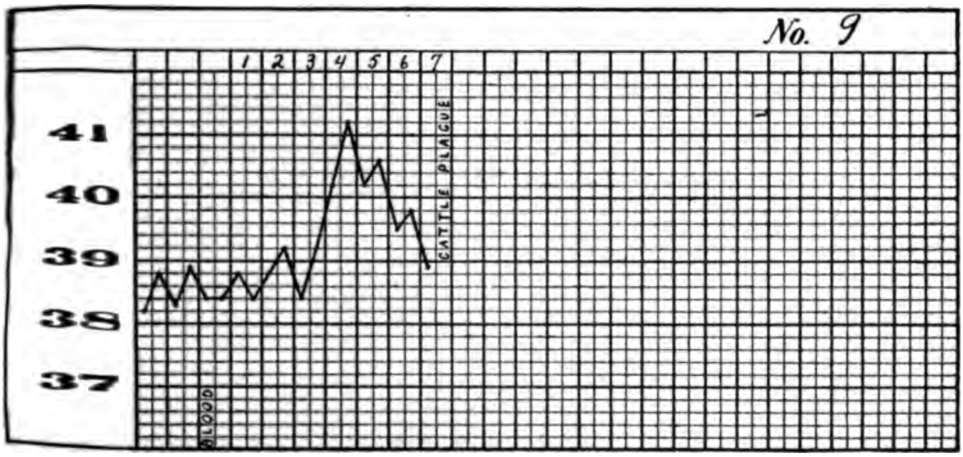
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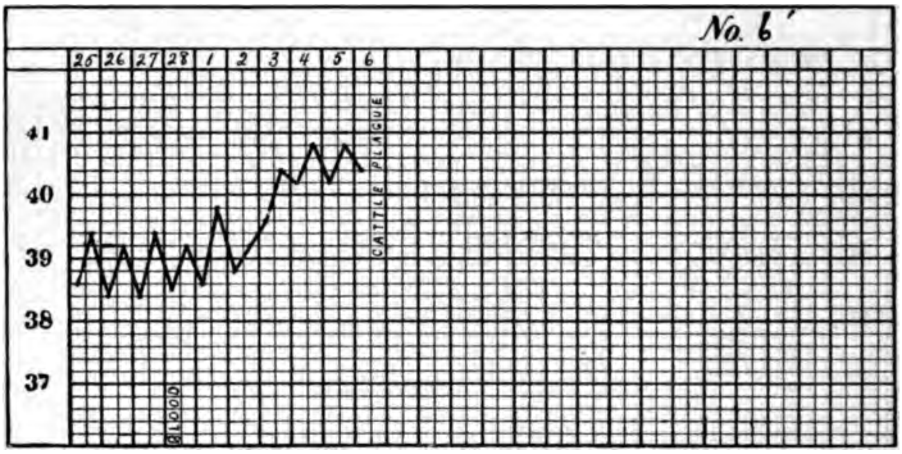
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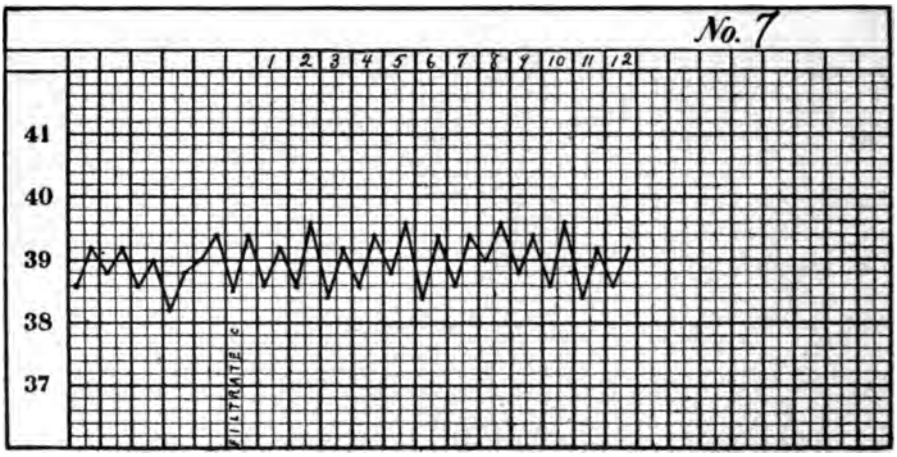
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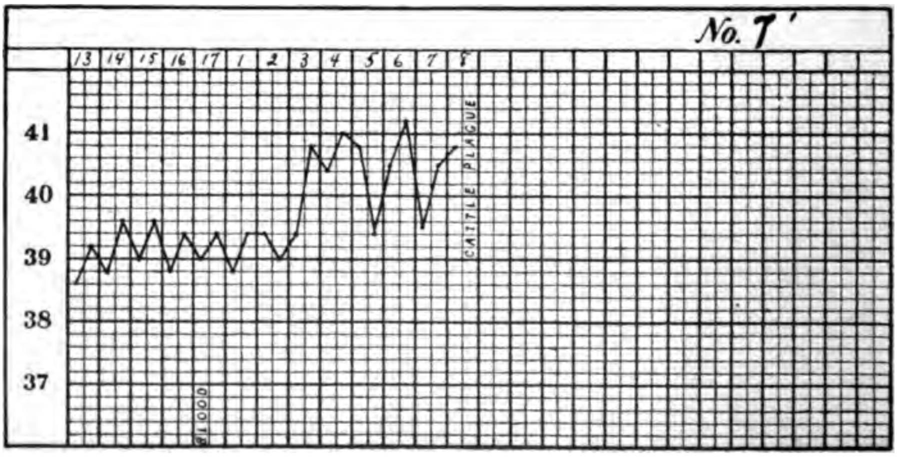
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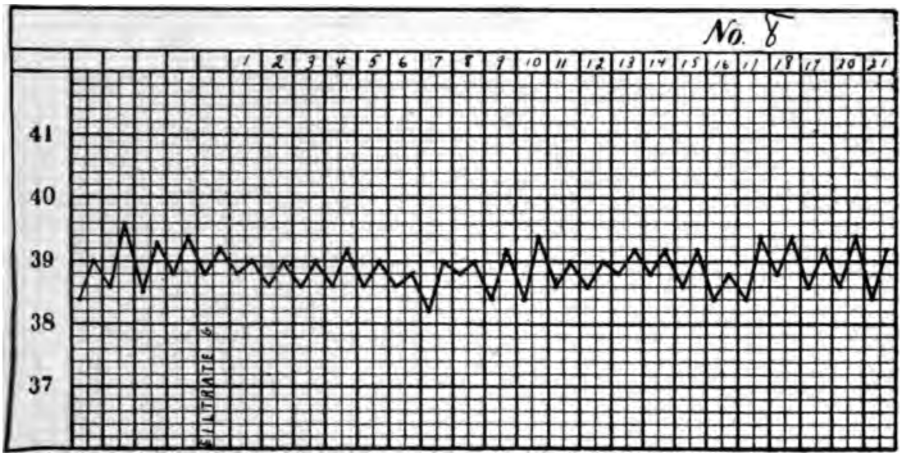
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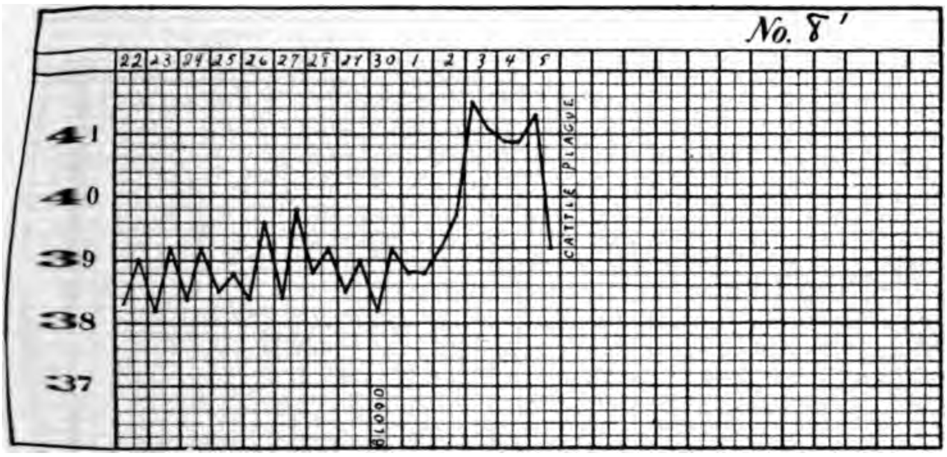
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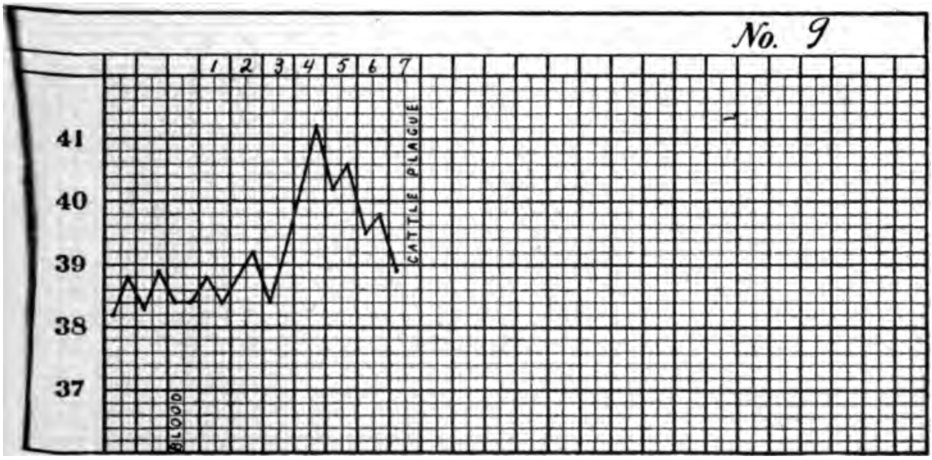
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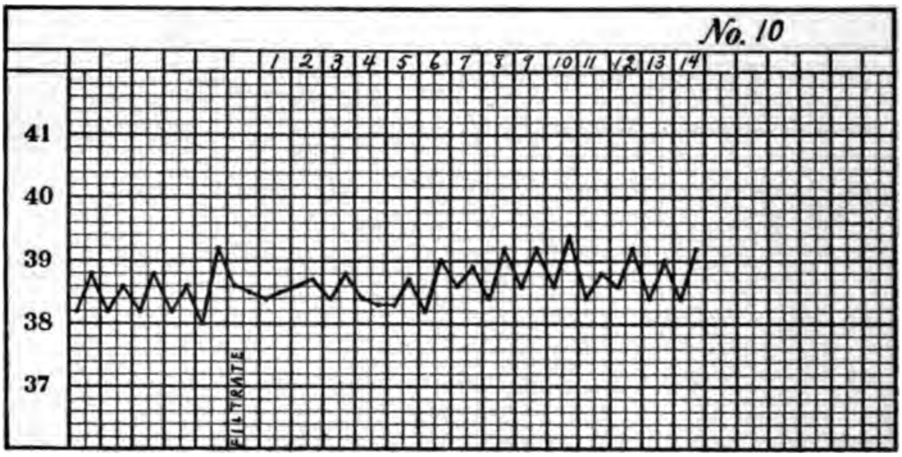
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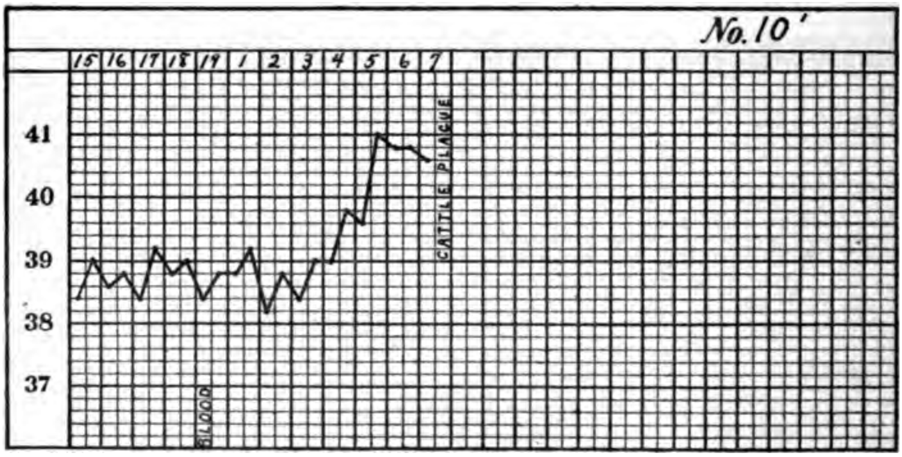
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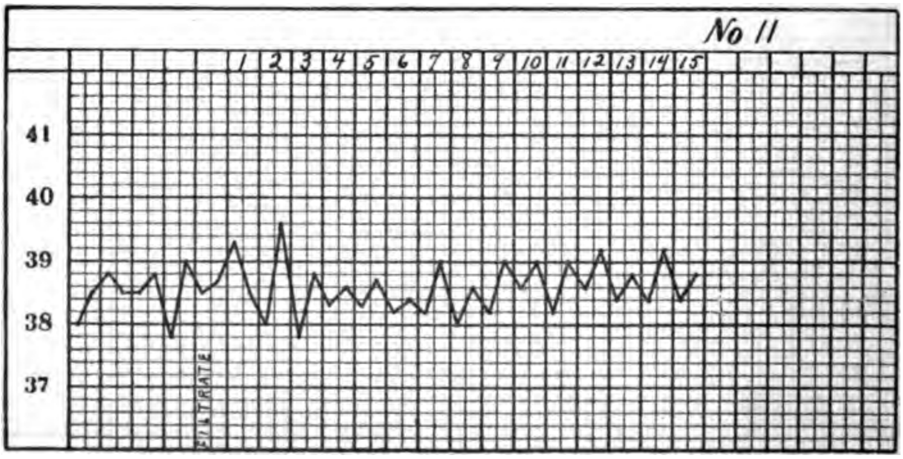
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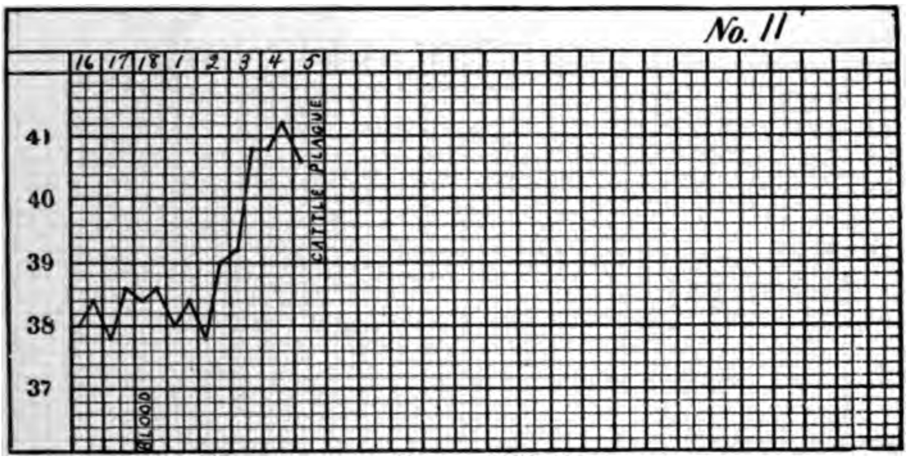
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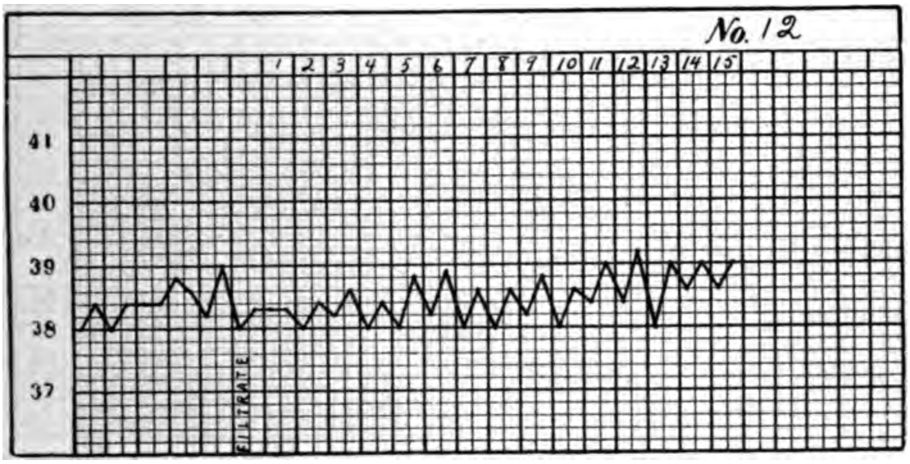
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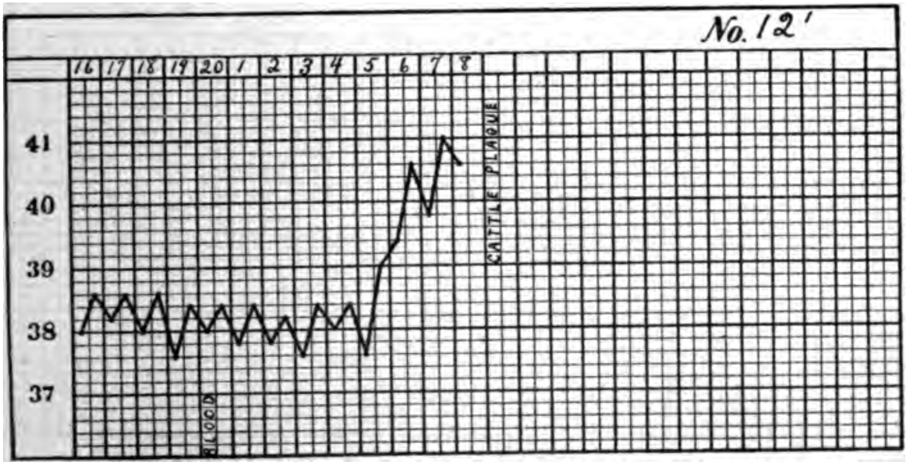
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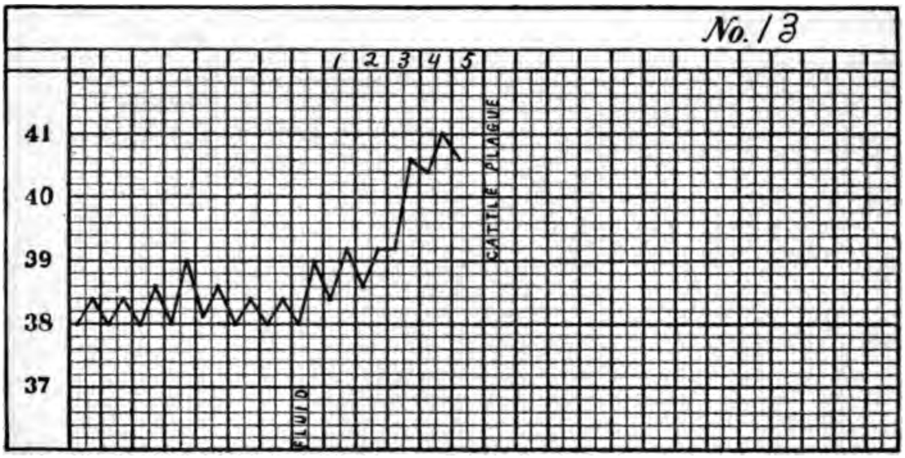
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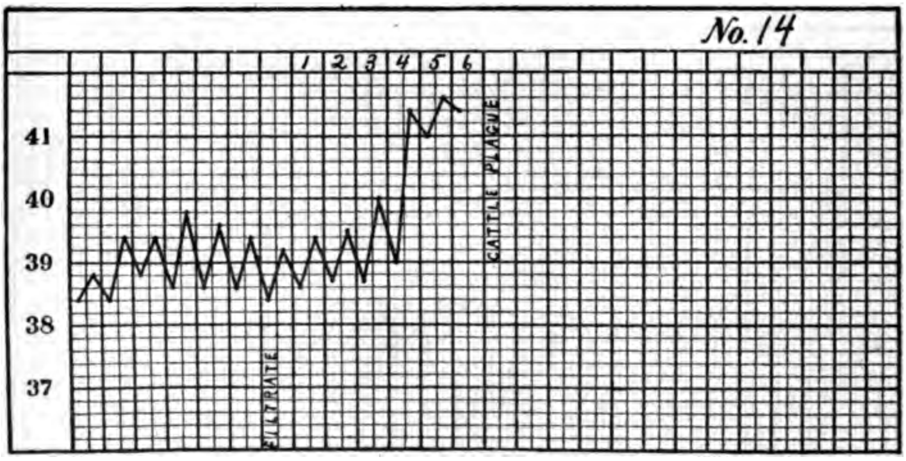
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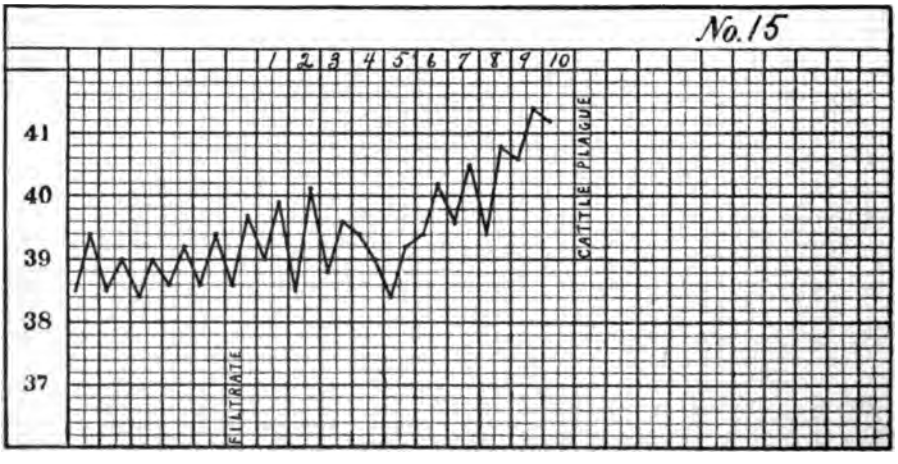
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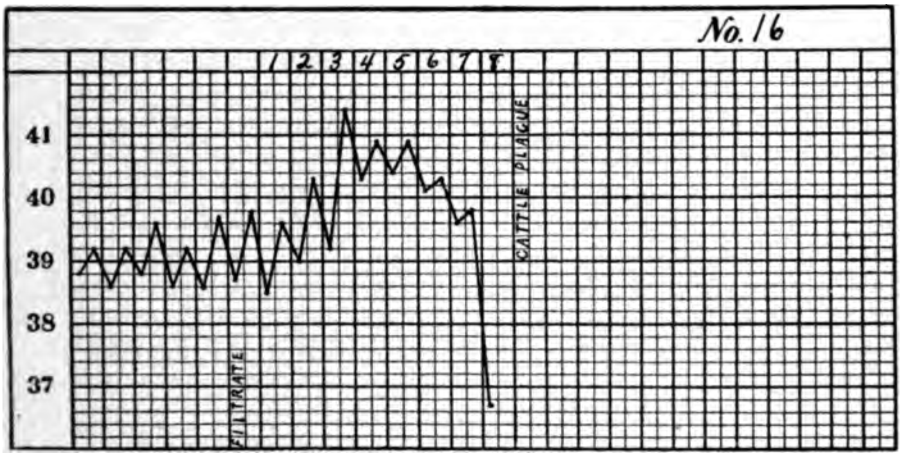
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EDITORIAL.

The unification of the medical interests of the Philippine Islands and the harmonizing of the respective attitudes of the American and Filipino physicians has been steadily going on for a number of years.

The Philippine Islands Medical Association had its first annual meeting in 1903, with rather a small attendance and a limited number of papers for discussion. No delegates from other countries were present. Each succeeding year has brought out a larger attendance and a greater interest. In 1906 we had two representatives—one from Hongkong and one from Japan. In 1907 three delegates attended—one from Hongkong, one from Japan and one from China: In 1908 there were eleven, representing respectively: The Imperial Japanese Government, the Imperial Chinese Government, the Imperial Siamese Government, Ceylon, Saigon, the Federated Maylay States, Singapore, and Hongkong.

At the fifth annual meeting, a representation comprising many of the countries included in the so-called territory of the Far East was present and the time was thought to be ripe for the formation of the Far Eastern Association of Tropical Medicine, to meet once in two years upon the invitation of one of the Governments of the component countries. This movement we hope will cement together the medical and scientific fraternities of the territories in question, will stimulate investigation and in addition will bring the center for the publication of research work in Far Eastern tropical medicine where it belongs, namely to some Government or society in the Orient.

Oriental medicine is undergoing a rapid expansion and is attracting increased attention throughout the world. Oriental governments are dealing with peoples whose prejudices and traditions work against the general scientific application of the art of medicine. This attitude must gradually be changed, but the results to be expected are sufficiently great to warrant the outlay of the best energies of the most prominent scientific workers of the world. It means nothing less than an improved hygienic understanding among Oriental peoples and the gradual removal of the causes which underlie certain phases of their stagnation. It will be accompanied by a general movement towards an enlarged sphere of activity among the people. The papers read at the Fifth Annual Meeting of the Philippine Islands Medical Association will be printed in this JOURNAL during 1908 and the discussions on the various topics will be given in its editorial columns. By this system readers can not only become familiar with the experimental data, but also with the opinions of physicians in this portion of the globe.

PAUL C. FREER.

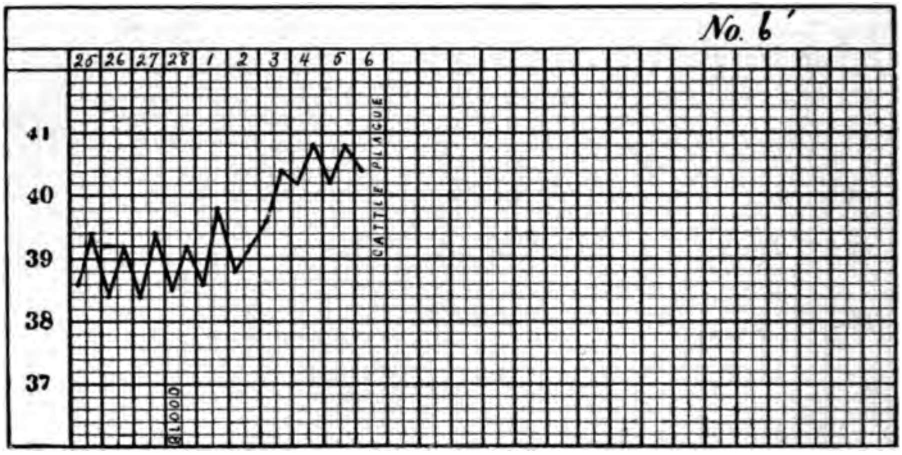
DISCUSSION ON THE PAPERS BY DR. VICTOR G. HEISER AND DR. HARRY T. MARSHALL.

Colonel L. M. Maus, deputy surgeon-general, United States Army: It affords me much pleasure to have occasion to express myself in regard to the practical conditions involved in the spread of cholera, as I had abundant opportunity during the early part of the epidemic in 1902 to study some of the channels of the dissemination of the disease. The history given by Dr. Heiser in regard to its origin agrees exactly with my own experience; it seems to be as nearly a correct one as we could find it to be at that time. A ship's cargo of cabbage came to Manila at the time mentioned and as the health office of Hongkong had notified us of the occurrence of the disease in that city, the Marine-Hospital Service was enabled to reject the shipment, which was dumped into the bay, but notwithstanding, several heads reached the beach at the Farola district and cholera developed. I remember the first case distinctly. It was sent to the San Juan de Dios Hospital; several others soon followed. A number of the members of the medical profession capable of making an accurate diagnosis were present. Cultures were taken from the bowels on the same night and the vibrio was observed under the microscope, but the final diagnosis was not completed until twenty-four hours later. The fact that the cases showed the cholera vibrio to be present and the further fact that there had been no cholera in the Islands up to that time, proved that the disease was imported. As you all know, the provinces were thoroughly supplied with medical officers when the epidemic of 1902 appeared, so that at that time, if there had been any disease in the Archipelago similar to cholera it would have been reported at once, and for that reason I am willing to say that cholera was not present in the Islands at the time of the outbreak in 1902. I believe therefore that the disease in this epidemic was imported *de novo.* It was brought from Hongkong, and spread from the Farola district.

The vibrio of cholera secretes a very virulent toxin. In the course of successive generations of the organism, the infections become milder. It should be noted that the vibrio which was introduced at the beginning of the epidemic in March, 1902, was of the most virulent character. I believe the infection spread largely from fæcal matter through the intervention of flies. Typhoid was stated to be a water-borne disease. In 1898, 300,000 soldiers went to the Spanish-American War, and the medical officers had some knowledge of the results which appeared during the campaign. A large percentage of the troops was infected with typhoid, and we found the soldiers to acquire the disease not only by means of the drinking water, but also by the spread of the organism through the intervention of flies, and I believe cholera to be disseminated in the same way, by flies contaminating the food. It is well known that the natives of the Philippines largely eat with their fingers from a common dish and this custom conduces to the spread of the disease. Owing to their defective habits of personal hygiene, many of the natives have their fingers infected. It is easy to see that their fingers may carry millions of microbes. Flies which carry the fæcal deposits on their feet can take the infection into the markets and thus spread the disease. Anyone who goes into a large military camp in the field will notice that the closets at meal times are frequently free from flies. At meal hours the insects transfer themselves to the tables. This is a fact, and therefore it seems to me that flies in the Philippines also leave the fæcal deposits at times in order to reach the more refined food of the natives. In spite of the general use of distilled water, the wells being closed after the beginning of the outbreak of 1902, little difference in the number of cases was observed. The disease ran its course. I believe the cases now present in the Islands to be sporadic, and that cholera is now endemic.

Dr. Clements, Bureau of Health: It seems to me that the burden of proof in regard to the presence or absence of cholera in the Philippines is upon the man who believes that cholera has disappeared. The great world center of cholera is in the Ganges Valley. I have never been there, but it would seem that the conditions in that region are climatically the same as in this Archipelago. The people are of a comparatively low order of civilization, with very primitive ideas of domestic hygiene living on low, filled lands, no winter breaks the seasons and a very large population is crowded into the area. We are practically certain that cholera never disappears from the Ganges Valley. Therefore I believe that those who maintain that the disease has disappeared from the Philippines must prove this to be the case. Cholera in my belief has been here all the time since it was first introduced. The native in some respects has a fairly good clinical eye. The lowest class of natives know smallpox and measles just as well as we do and these infections have native names. On the other hand, cholera and some other diseases which have been brought into the Archipelago in the early times of Christian occupation are known to the natives only by the Spanish designation, which to my mind is evidence that cholera was introduced since Spanish settlement and was unknown previously. I desire proof that it has ever disappeared after having been once introduced into the Philippines. I have done probably as much field work in connection with cholera as any other man in the Islands. I have been all over the Archipelago and mild cases of a disease which is exactly like cholera, except in the percentage of mortality, appear every year. I have been told this in every place I visited.

In regard to the epidemic of 1902 I think that some of the remarks which have been made here in reference to the probability of variability in the strains of pathogenic organisms are correct. It is very possible that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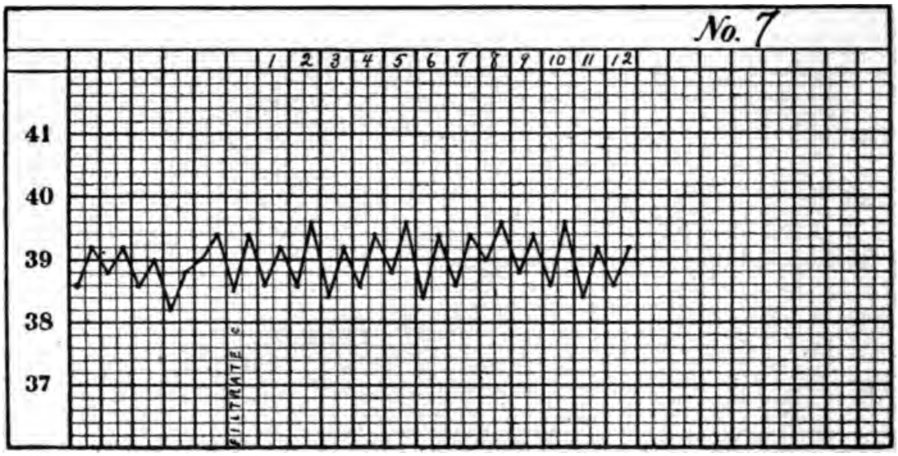
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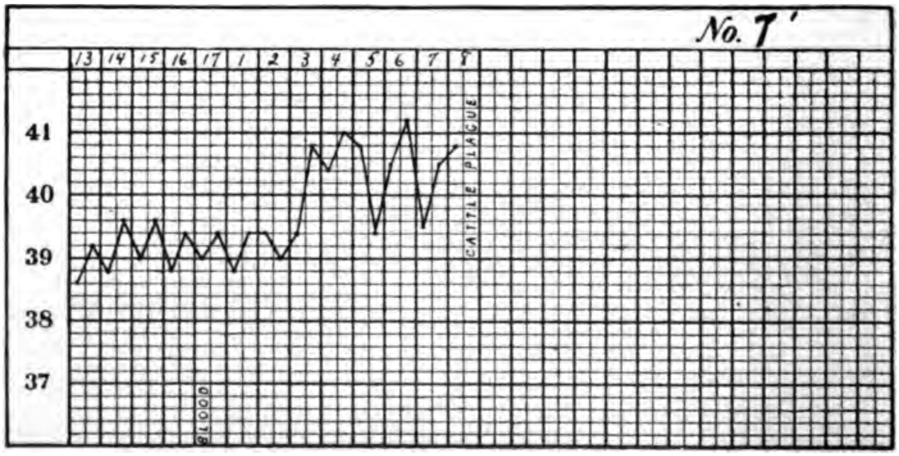
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food might easily become infected and become a means of propagating the disease.

Dr. Marshall, Biological Laboratory, Bureau of Science: In concluding I wish to call attention to one statement made by Dr. Heiser to the effect that the cholera vibrio does not seem to abate in virulence while passing through animals and he concluded that some external cause produced the fall of epidemics. My experiments prove that the virulence may diminish most markedly even under favorable conditions of passage through animals.

Ruffer has also shown that the virulence of bacteria, identical with cholera culturally and in other ways, is subject to great variation. In this connection I also wish to call attention to Dr. Clements's statement and emphasize the extreme rapidity with which variation from nonvirulent to virulent bacteria may take place. In experiments with organisms of dysentery a nonagglutinating variant can be produced within the space of a few hours.

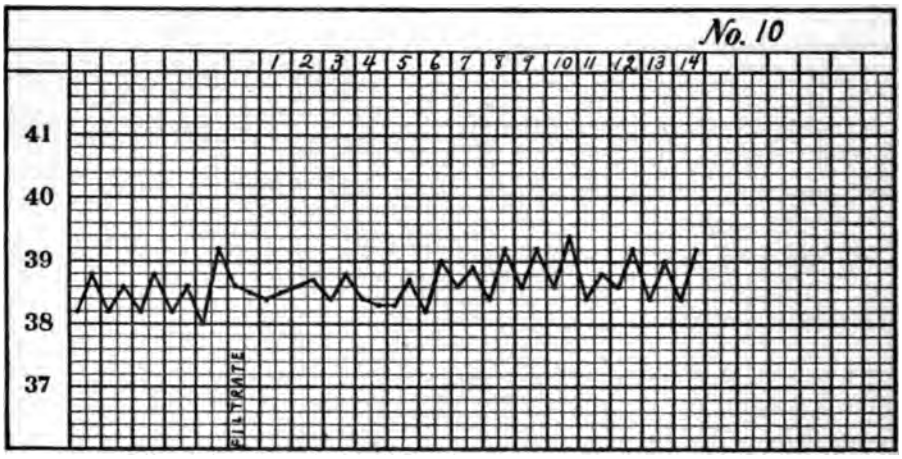
Dr. Heiser's hypothesis of gradual immunization through repeated infections with mild or nonvirulent strains of cholera is interesting, but it can not be said at present whether this is a feasible means of immunization or not, possibly, a local immunity of the intestine may result, but the observations do not show that a general immunity may follow. The results of the ingestion of bacteria or of toxins are not conclusive.

In referring to some remarks made by Dr. Musgrave I wish to state that it is usual for the cholera vibrio to be killed in the presence of ordinary saprophytic bacteria, and it is usually stated that it dies rapidly in sewers. I have not encountered in the literature accounts of any experiments in which a symbiotic condition favorable for cholera has been developed.

DISCUSSION OF THE PAPER BY DR. EDWARDS.

Captain Ryley, R. A. M. C., Hongkong: When an epidemic occurs in tropical countries it is usual for the people to drink distilled water or soda water. I inoculated soda water artificially with cholera organisms, and I found that the usual pressure of about 150 pounds to the square inch, which it is believed should destroy pathogenic bacteria, had no effect on the cholera vibrio. The soda water was of the variety which is made by impregnating the water with carbonic-acid gas. I was able to recover the cholera organism from the water which I worked with.

Dr. Carpenter, United States Navy: At the Cavite Naval Station for the past year we have had experience with artesian well water. We found that the water which came from a depth of 508 feet was infected when it first came through the pump and we began to employ boiled water. This was not sufficient to supply several thousand people and we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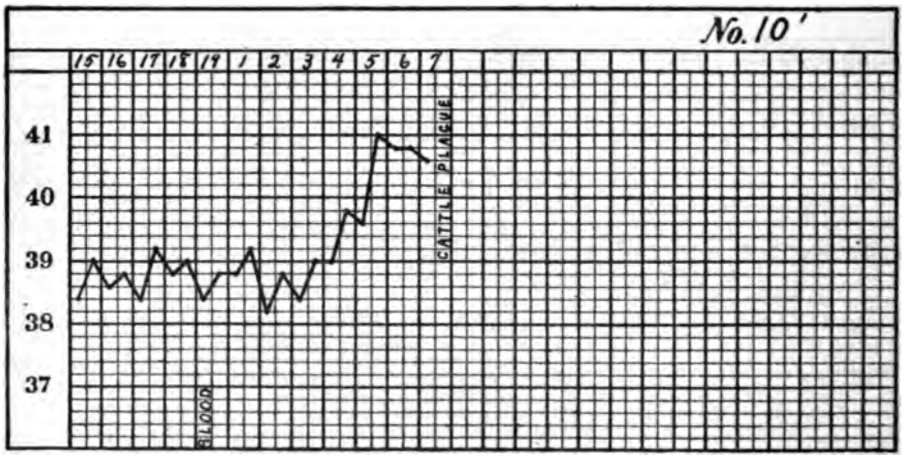
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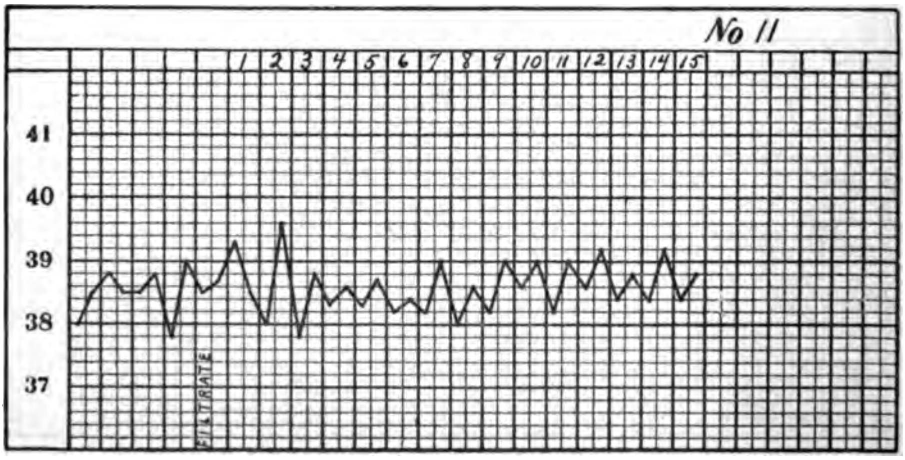
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REVIEWS.

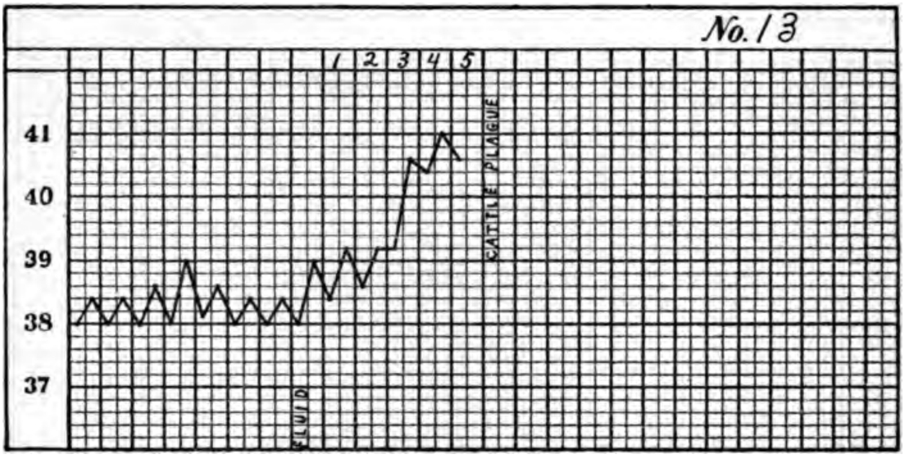
The Treatment of Disease, a Manual of Practical Medicine. By Reynold Webb Wilcox, M. A., M. D., LL. D. Cloth. Pp., xxviii+911. Price $6. Philadelphia: P. Blakiston's Son & Co., 1907.

Comparative Anatomy of Vertebrates. Adapted from the German of Dr. Robert Wiedersheim by W. N. Parker, Ph. D. Third edition, founded on the sixth German edition. With three hundred and seventy-two figures and a bibliography. Cloth. Pp. xii + 576. Price $3.75 net. New York: The Macmillan Company, 1907.

The scope of this work is limited to what is signified in its title, and the subject is treated tersely and clearly from the standpoint of evolution. After the introduction, which gives a synopsis of the early stages of development in general, the different systems are presented briefly with definitions of terms beginning with the integument followed by the skeleton, muscles, etc.; then each system is described as found in *Amphyoxus,* in fishes, in amphibians, in reptiles, in birds and in mammals. The arrangement is simple and convenient for students in its use as a text book. Many excellent, well-selected drawings increase its efficiency. A ready index and a bibliography add to its value as a reference work, although meager in details and too brief to be of great value to investigators. The style is clear and limpid, concise and pointed as a rule, but there are obscure passages that need reconstruction, as for example on page 122, beginning with line 2. "The cranial cavity has become further enlarged at the cost of parts formerly situated extracranially than is the case among Reptiles."

The emphasis placed on evolution necessitates ontogenetic and phylogenetic details and paleontological records that force the question as to the reason for many striking similarities of extinct forms to existing ones, and of these to each other in both the development of the individual and of the race. Is this similarity to be explained by evolution, or is it only a matter of the same laws controlling development, so that in one this development reaches beyond the point of its cessation in others, thus leaving traces of the early stages as rudiments, vestiges, degenerations, etc.? The latter explanation is as plausible and workable as the former, and does not require "blood relationships of animals in general" as a factor.

The treatment of the segmentation of the ovum is crude and simple. It might have been improved by a few plates illustrating the various steps of cell cleavage by mitosis.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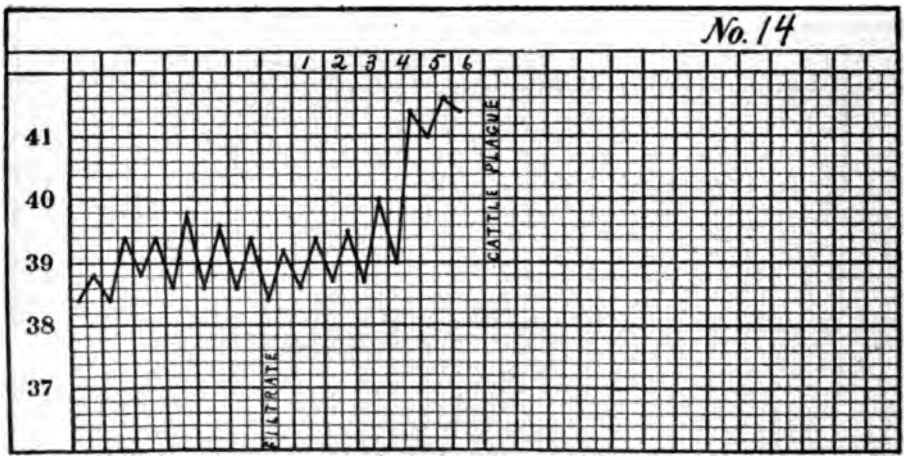
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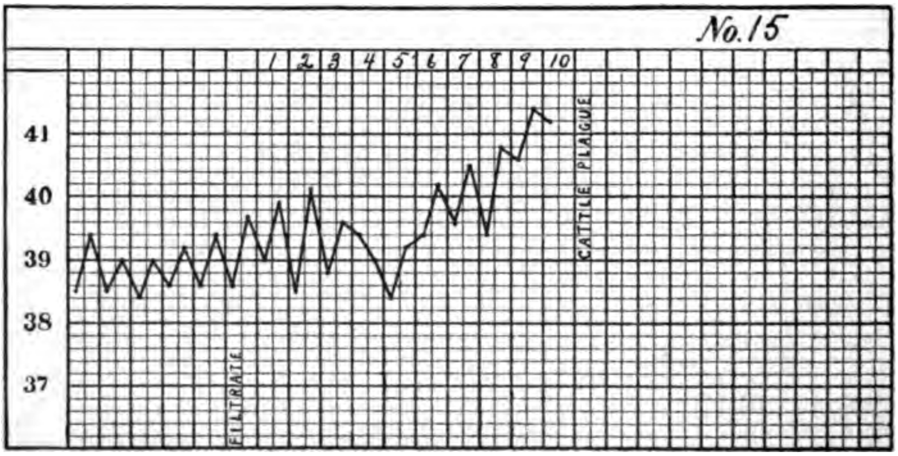
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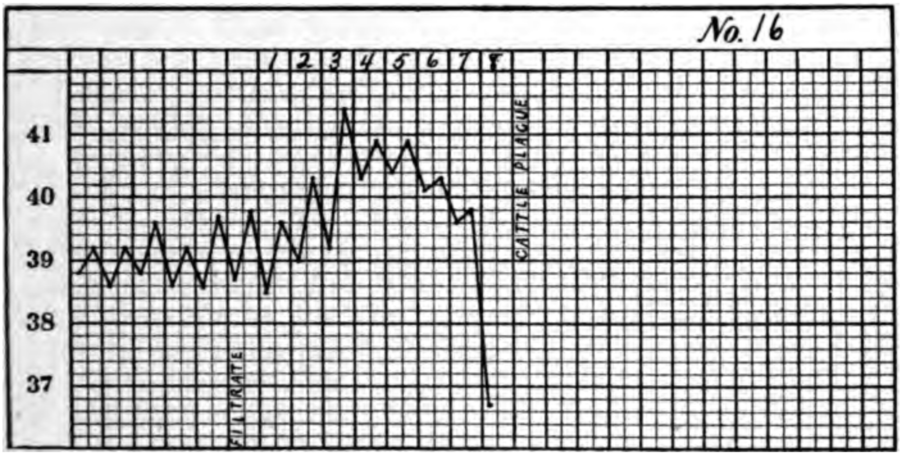
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Harry M. Ickis, E. M.

DIVISION OF MINES
BUREAU OF SCIENCE

April the first
1908

THE PHILIPPINE

JOURNAL OF SCIENCE

B. MEDICAL SCIENCES

VOL. III JULY, 1908 No. 3

THE PREVALANCE AND DISTRIBUTION OF THE ANIMAL PARASITES OF MAN IN THE PHILIPPINE ISLANDS, WITH A CONSIDERATION OF THEIR POSSIBLE INFLUENCE UPON THE PUBLIC HEALTH.[1]

By PHILIP E. GARRISON.[2]

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

Summary of results.

Examinations and infections.	Number.	Per cent.
Prisoners examined	4,106	------
Prisoners infected	3,447	84
Whipworms (*Trichuris*)	2,426	59
Hookworms	2,135	52
Eelworms (*Ascaris*)	1,052	26
Amœba	926	23
Other intestinal protozoa (ciliates and flagellates)	853	21
"Cochin-China diarrhoea worms" (*Strongyloides*)	132	3
Pinworms (*Oxyuris*)	32	0.8
Tænia	30	0.7
"Japanese lung flukes" (*Paragonimus*)	18	0.4
"Japanese blood flukes" (*Schistosoma*)	16	0.4
"Japanese liver flukes" (*Opisthorchis*)	11	0.3
The "dwarf tapeworm" (*Hymenolepis*)	5	0.1
Total infections	7,636	186
Intestinal worms only	5,812	142
Flukes	45	1.1
All intestinal protozoa	1,779	43

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[1] Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, Manila, February 27, 1908.

[2] Assistant surgeon, United States Navy; detailed medical zoölogist to Biological Laboratory the Bureau of Science, Manila, P. I.

INTRODUCTION.

The present paper reports the results of a statistical investigation concerning the prevalence of animal parasites among the Filipinos, conducted through the year 1907, for the purpose of obtaining accurate knowledge which would serve as a guide to some definite conclusions with regard to the importance of animal parasites and more especially of intestinal worms in the Philippines, and of their possible influence as a factor in determining the hygienic and industrial status of the Filipino people.

In examining the fæces for these infections, diagnoses were made not only of protozoäl and verminous infections of the intestine, but of infections in other organs with worms the ova of which escaped by means of the intestinal tract. Therefore, the investigation was made upon those animal parasites the infection with which could be diagnosed by examination of the fæces and included in addition to parasites of the intestine, certain forms living in the liver (*Opisthorchis, Fasciola,* etc.), the lungs (*Paragonimus*), and in the veins or arteries of the lower part of the intestinal tract (*Schistosoma*). Accordingly, while the expression "intestinal parasites" would include most of the species considered, the presence of infections with forms not of the intestine, which it was highly desirable to retain in our statistics, made it necessary to employ in the title the broad term of "animal parasites" and to limit its scope as has been indicated.

MATERIAL.

A most favorable field for the investigation presented itself at Bilibid Prison where a changing population of about 3,500 prisoners from all parts of the Islands was available for examination and where the routine miscroscopic examination of fæces was already established.

The great majority of the prisoners were adult male Filipinos, but some native women, a number of Chinese, and a few Americans were among the cases examined.

Almost all of the population of the prison was examined during the year, the entire work including a total of 4,106 persons. Prisoners newly admitted were subjected to examination at once in quarantine, while the others were placed in a special ward until specimens of fæces could be obtained and studied. In addition, examination was made of the stools of all prisoners admitted to the prison hospital for other causes.

Specimens were taken from fresh stools obtained after the subject had been given a dose of magnesium sulphate. The necessary number of daily examinations made it impossible to study more than one coverglass preparation from each specimen and if no infection was detected the individual was dismissed without further examination. Cases requiring treatment were kept in the hospital and antihelmintics were administered repeatedly until two examinations for *Ascaris* or three for hookworms proved negative. The inadequacy of an examination based on a single cover-glass preparation was fully recognized, and was repeatedly proved by instances in which the first examination showed only one infection while subsequent ones revealed several. It is to be assumed that since many individuals gave negative results at first and were not again examined, many infections escaped diagnosis and that the figures given are below the number of infections actually present in the 4,106 prisoners.

A selection of cases presents itself because the prisoners were all adults and nearly all males. The results of the work of a number of authors, publishing in the aggregate upon about 10,000 cases, have shown fairly conclusively that with the exception of a few species, the percentage of infection with animal parasites is higher in children than in adults, and in females than in males. Hence it would appear in this connection also that the figures presented by the Bilibid prisoners are a minimum if taken as an index of infection in the population as a whole.

Aside from the question of sex and age, it is probable that the prisoners at Bilibid are fairly representative of the general population, coming as they do from the various provinces scattered throughout the Islands and from all classes of society, although the lower laboring class may have been present somewhat in excess of the proportion which it holds in the mass of the people.

The institution of this investigation and the recording and compilation of the data obtained for this study were entirely the work of the author. About 7,000 of the 15,000 examinations entering into this work were made by Dr. Ralph T. Edwards, who was in charge of the Bureau of Science routine work in clinical microscopy at Bilibid. Frequently prisoners were examined and treated by Dr. E. C. Shattuck,[3] resident physician at Bilibid, before the examination by the Bureau of Science was made, and in order that our record of infections for each patient might be complete, Dr. Shattuck has kindly allowed me to use the results of about 5,000 examinatons which he made upon these 4,106 prisoners either before or after their examination by Dr. Edwards or myself.

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[3] Shattuck, *Amer. Med.* (1907) 13, reporting upon uncinariasis in Bilibid Prison, particularly with regard to its diagnosis and treatment, states that as the result of approximately 1,000 examinations he found 243 cases of uncinariasis, 63 of amœbic dysentery, 3 of *Balantidium coli* infection, 186 of ascariasis and 7 of tæniasis. Shattuck's work was done from a clinical rather than statistical viewpoint, and he has kindly given us his coöperation in our effort to establish the actual frequency with which infection with animal parasites prevails among the Filipinos.

Since the work of accurately determining the specific identity of the parasites found is still in progress; since in many cases it is impossible to make more than a generic diagnosis from the ova alone and since further, the medical and sanitary interests involved are, with few exceptions, identical for different species of the same genus, we shall use only generic names throughout the present paper.

In addition to the microscopic findings, a record was kept of the province from which each prisoner came, with the object of discovering any inequalities in the geographical distribution of infections which might be of practical value with regard to the establishment of sanitary procedures in the Islands.

GENERAL RESULTS.

Of the 4,106 prisoners examined, 3,447 were found to be infected with one or more species of animal parasite, an average of 84 per cent. The total number of infections was 7,636, an average of 186 infections for each 100 prisoners examined.

Unfortunately we know of no statistics for tropical countries, based upon an adequate number of examinations, which are suitable for close comparison with these figures for the number of infected persons. The Anæmia Commission of Porto Rico reported 100 per cent of the persons which were examined to be infected with hookworms, their work being directed purposely to that parasite and their report not being upon a true statistical basis for the general population. Dobson and Fearnside, in India, give the number of infections found, but fail to state the number of persons infected. Calvert, in India, found 92 per cent infected, but examined only 100 men.[4]

The total number of infections reported by these authors is as follows:

Authority.	Date.	Country.	Number examined.	Number of infections.	Per cent.
Anæmia Commission	1904	Porto Rico	4,482	6,259	139.64
Calvert	1901	India	100	143	143
Fearnside	1900	do	878	921	104.90
Dobson	1893	do	1,249	1,340	107.28

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[4] For complete bibliographical references to authorities quoted in the present paper see Stiles & Garrison; A Statistical Study of the Prevalence of Intestinal Worms in Man: *Bull. Hyg. Lab., U. S. Pub. Health & Mar.-Hosp. Serv.*, Wash. (1906), **28**, 74–77.

As might be expected, the figures for temperate climates are not so high. However, the following authors have reported an average of over 50 infections for each 100 persons examined:

Authority.	Date.	Country or place.	Number examined.	Number of infections.	Per cent.
Cima	1893, 1896	Italy	[a]110	87	79.08
Gubareff	1896	Russia	486	371	76.32
Gribbohm	1872-1877	Kiel, Germany	[b]972	717	73.81
Heller	1872-1875	do	[b]611	437	71.52
Heisig	1893	Griefswald	230	140	60.85
Grusdeff	1892	Kostroma, Russia	260	143	55

[a] Children. [b] Autopsy examinations.

While it could not be argued, perhaps, from a comparison of statistics, that the population of the Philippines is necessarily more generally infected with animal parasites than the people of certain other localities for which figures almost as high have been published, the fact remains that the average number of infections per 100 persons (186) found in examining the 4,106 prisoners at Bilibid, is higher by over 40 than has ever been definitely reported for any other country upon a number of cases sufficiently large to be taken as a fair index to the prevalence of animal parasites in the general population.

PARASITES PRESENT.

The infections represented at least fifteen genera and probably about twenty species. The genera positively determined were the two hookworms, *Necator* and *Agchylostoma;* the common "round worm," *Ascaris;* the common whipworm, *Trichuris;* the common pin or seat worm *Oxyuris;* the worm of Cochin-China diarrhœa, *Strongyloides;* the cestode genera *Tænia* and *Hymenolepis;* the Japanese lung fluke, *Paragonimus;* the Japanese liver fluke, *Opisthorchis;* the Japanese blood fluke, *Schistosoma,* and the four protozoäl genera, *Amœba, Balantidium, Lamblia, and Cercomonas;* in addition, there were a number of undoubted infections in which the identity of the parasites was not even generically determined.

MULTIPLE INFECTIONS.

Multiple infections were numerous, as is shown by the fact that 7,636 infections were distributed among the 3,447 infected prisoners, an average of 222 infections to each 100 infected persons, or nearly 2.25 infections per infected idividual.

One thousand and sixty-seven, or slightly more than one-fourth of the prisoners examined, showed infection with one species of parasite only; of these single infections, 428 were with hookworms, 384 with whipworms, and the remaining 255 with other species.

Nine hundred and thirty, or slightly less than one-fourth of the persons examined, showed a double infection, of which hookworms and *Trichuris* gave 518, or about one-half, *Ascaris* and *Trichuris* nearly one-fourth, and various combinations the remainder.

Seven hundred and twenty-three, or about 18 per cent, had triple infections, of which the most common was with *Ascaris*, hookworms and *Trichuris;* although combined infections with *Amœba*, hookworms and *Trichuris* and with hookworms, *Trichuris* and flagellates were present with almost equal frequency.

Three hundred and sixty-six prisoners, or 9 per cent, were infected with four different parasites, the most common combination being *Amœba*, flagellates, hookworms and *Trichuris*.

One hundred and thirty-one prisoners (3 per cent) gave a combined infection with 5 parasites, 80 of which were with *Amœba*, flagellates, *Ascaris*, hookworms and *Trichuris*.

A combination of six different infections in one patient occurred fifteen times; in five of these cases the parasites were *Amœba*, flagellates, *Ascaris*, hookworms, *Strongyloides* and *Trichuris*.

Two prisoners had seven separate infections, and one man was infected with nine different parasites, the combination in the last case being *Amœba*, flagellates, *Balantidium*, *Ascaris*, hookworms, *Strongyloides*, *Trichuris*, *Opisthorchis* and *Schistosoma*.

GEOGRAPHIC DISTRIBUTION.

A rather elaborate attempt was made to determine whether the individuals coming from any particular part of the Islands gave an excess of infection over those from other sections. To this end, a record of the previous residence of prisoners was taken and the infections found were tabulated by separate provinces, separate islands and various groups of provinces and of islands. No significant difference in the total percentage of infection could be detected. Prisoners from the extreme northerly provinces presented about the same percentage (with all parasites) as did those from the Visayas or from central or southern Luzon.

The same even geographic distribution seemed to prevail for each separate species of parasite, with the exception of infections with the three trematode genera, *Paragonimus, Schistosoma* and *Opisthorchis,* especially the two former, which appeared to originate almost exclusively in certain of the southern islands.

The distribution of the infections with the three trematodes mentioned will be considered more in detail under each genus.

While practically all parts of the Islands are fairly well represented at Bilibid, an investigation conducted at such long range would be able to discover none but very marked inequalities in the distribution of the parasites and it is by no means excluded that further work, done in the various provinces themselves, would indicate an excess of infection in certain parts of the Islands, which did not appear among the prisoners examined at Bilibid.

INFECTIONS WITH TRICHURIS.

(59 per cent.)

If we confine ourselves to statistical reports based upon an adequate number of cases (several hundred), much higher percentages of infection with whipworms have been published for temperate than for tropical climates.

The highest rate of infection with *Trichuris* definitely reported was found by Heisig in Germany in 1893 (45.21 per cent); the next, by Gubareff in Russia, in 1896 (43.62 per cent). In these cases, the total percentages of infections with all intestinal worms were only 60.85 and 76.32, respectively. Boycott in 1904 reported 38.78 per cent of whipworm infections from Cornwall, England, but only 98 men were examined. Grechaninoff (1890) found this parasite in 26.41 per cent of 583 persons examined in St. Petersburg. Other German statistics for whipworms are: Sievers, Kiel, 1887, 2,629 persons examined, 19.81 per cent infected; Roth, Bale, 1877–1880, 752 persons examined, 23.67 per cent infected; Gribbohm, Kiel, 1872–1877, 972 persons examined, 32.20 per cent infected; Heller, Kiel, 1872–1875, 611 persons examined, 30.60 per cent infected; Müller, Erlangen, 1862–1873, and Dresden, 1852–1862, 1,755 and 1,939 persons examined and 11.11 and 2.57 per cent infected, respectively.

Stiles and Garrison (1906) in examining 3,457 persons in the United States found 7.72 per cent to be infected with whipworms.

Cima (1893 and 1896) in the vicinity of Naples, Italy (subtropical), found 37.27 per cent of infection in examining 110 children.

On the other hand, we have the following statistics for whipworms from populations in the tropics: Anæmia Commission, 1904, Porto Rico, 4,482 persons examined, 7.27 per cent infected; Daniels, 1901, British Central Africa, 251 examined, 2.79 per cent infected; Fearnside, 1900, India, 878 examined, 6.95 per cent infected; Dobson, India, 1893, 1,249 examined, 4.40 per cent infected.

While estimates have been made regarding the frequency of whipworm infection in different populations ranging from 50 per cent (in Italy)[5] to 100 per cent (in Paris)[6] it appears that our figures for the Philippines (59 per cent) give a higher rate of infection with this parasite than has ever been definitely reported upon a number of cases sufficiently large to serve as an index to the general population.[7] This fact would seem to give fairly conclusive proof to the view that the relatively low rates of infection with whipworms reported from the tropics are due to the failure of workers in tropical countries to record whipworm infections.

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[5] Blanchard, Raphael: Traite De Zoölogie Medicale. Paris (1889), 1, 785.

[6] Braun, Max: Die Thierischen Parasiten. Würtzburg (1903), 277.

[7] Estimates of the frequency of infection, without actual statistical proof, would appear to be absolutely unreliable. While from 50 to 100 per cent of the population of southern Italy was estimated to harbor whipworms, Cima's examination of 110 children gave only 37.27 per cent of infection. *Ascaris* had been estimated to be the most common intestinal parasite of man in the Philippines, but actual statistics show it to be about one-half as frequent as whipworms or hookworms. When the present investigation had proceeded to the examination of 1,000 patients, the author estimated that the percentage infected with whipworms would approach very nearly to 90, and even expressed such an opinion in a meeting of the local medical society; our final figures show only 59 per cent.

A number of authors[8] have found whipworm to be more common in females than in males and in children (under 15 years of age) than in adults and therefore it is probable that the actual frequency of the parasite in the Philippine population as a whole is higher than is shown by our figures, which are exclusively based upon the examination of adults and almost exclusively of males.

So far as could be determined from the records of the previous residences of the prisoners examined, the percentage of infections with whipworms appears to be about equal throughout the different provinces of the Islands.

INFECTIONS WITH HOOKWORMS.

(52 per cent.)

Hookworms, after *Trichuris*, were the parasites most frequently encountered (52 per cent). Much higher rates of infection with hookworms have been reported from other countries, but some of these, notably those detailed in the report of the Porto Rican Anæmia Commission, are not suitable for purposes of comparison, for the reason that the examinations were primarily directed to the study of hookworms, while in our own work hookworm infections were recorded no more faithfully than were those with other parasites.

Calvert, Fearnside and Dobson in India reported 83 per cent, 65.83 per cent, and 75.58 per cent, respectively, and with the exception of their comparatively low rates of infection with whipworms, these authors appear to have recorded all intestinal verminous infections impartially—their rates of total infections being 143, 104.9 and 107.28 per cent, respectively.

The recognized pathogenicity of hookworms, their relatively great importance from the view point of clinical medicine and public hygiene, and the seriousness of the problems presented by uncinariasis in other countries, urge us to depart here from a purely statistical presentation of the case and briefly to consider the clinical aspect of hookworm disease in the Philippines, so far as we have been able to determine it by observation and inquiry during the past year, in relation with the apparent frequency of hookworm infections.

While our figures show 52 per cent of the 4,106 prisoners which were examined to be infected with hookworms, clinical manifestations of uncinariasis were rare; in fact, cases of severe anæmia, in the absence of tuberculosis, malaria, or other anæmia-producing diseases, were practically absent. While hundreds of patients come from the provinces to the hospitals of Manila annually, general inquiry among the physicians elicits the information that although hookworm infections are common, they are usually first diagnosed in routine examinations of the fæces and if severe anæmia is present, a concurrent infection of malaria, tuberculosis or of some other disease which would account for the condition exists. Furthermore, after careful and general inquiry among numerous medical officers of the Army, Navy, and the Bureau of Health who had served or were serving in the provinces, we have failed to obtain any knowledge of any general or marked prevalence of hookworm disease among the natives.[9] Accordingly, while further investigation may discover a greater frequency of uncinariasis in its severer forms than now appears to be the case, it would seem to be reasonably certain that there is no such prevalence of this disease with severe manifestations among the natives of the Philippines as we might expect in view of the apparent fact that over one-half of the population harbors this parasite.

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[8] *Bull. Hyg. Lab., U. S. Pub. Health & Mar.-Hosp. Serv.*, Wash. (1906), **28**, 70–71.

Whether or not the explanation of this apparent rarity of clinical symptoms in hookworm infections among the Filipinos is a racial immunity on the part of the people to the toxins secreted by the worms, as has been suggested in regard to the similar condition found by Stiles in negroes in the Southern States, by the Anæmia Commission in Porto Rico and by Zinn and Jacoby in Africa, the fact that severe clinical manifestations of uncinariasis are rare in the Philippines materially alters the problem which is presented. Instead of producing an acute condition such as was presented in Porto Rico, St. Gothard Tunnel, the Westphalian coal mines, and in other places where uncinariasis prevailed in its severer forms, it would appear that in the Philippines hookworm infections play a part more nearly resembling that of the other common intestinal worms to which no definite pathology or severe symptomatology is usually attributed.

INFECTIONS WITH ASCARIS.

(26 per cent.)

Rates of infection with "round worms" have been reported ranging from 0.49 per cent (Stiles and Garrison, United States, 1906) to 50.97 per cent (Wellman, west Africa, 1904).

A compilation of statistics obtained from nearly 3,000 persons examined and reported upon by various authors, shows *Ascaris* to have been found almost twice as frequently in females as in males, as follows: Males examined, 1,732; infected with *Ascaris*, 138, or 7.97 per cent; females examined, 1,103; infected, 159, or 14.42 per cent.[10]

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[9] **The most severe case of hookworm disease seen by the author in Manila and the only one showing in a marked degree the cardinal symptoms of extreme anæmia, with cardiac murmurs, œdema, dyspnœa, and great weakness, was a Japanese male infected with the "Old World" hookworm (*Agchylostoma duodenale*).**

[10] ***Bull. Hyg., U. S. Pub. Health & Mar.-Hosp. Serv.*** Wash. (1906), **28,** 70–72.

A similar compilation with regard to age demonstrates that "round worms" are encountered with over twice as great frequency in children under 15 years than in adults of middle life, the number of children from 1 to 15 years examined being 2,381; those infected, 400, or 16.80 per cent; adults, from 15 to 50 years, examined, 1,461; infected, 107, or 7.32 per cent.

It is evident that our figures (26 per cent), based entirely upon adults and almost entirely on males, are considerably below the proportion of the total Philippine population harboring this worm, should a like sex and age relation with regard to *Ascaris* infections hold in the Philippines.

INFECTIONS WITH AMŒBA.

(23 per cent.)

Statistics regarding the frequency of *Amœbæ* in the human intestine have varied greatly in the percentage of infection found, numbers as high as 50 and even 70 per cent having been reported; a comparison is rendered more unsatisfactory by the fact that some authors have attempted to distinguish between ***Entamœba coli*** and ***Entamœba histolytica*** and others have not done so. In the work here reported no attempt at such differentiation was made after the investigation had progressed for a few weeks, for the reason that it was not found possible to differentiate the two species with any certainty in a routine microscopic examination of the fresh fæces, and also because we are of the opinion that, until more light has been thrown upon the problems of the specific identity and the relative pathogenicity of intestinal amœba, the only safe attitude to hold toward amœbic infection of the intestine in the Philippines is to consider all intestinal amœba potentially pathogenic and to treat them accordingly. In view of such an opinion, the practical purpose of the investigation expressed in the introduction would be served by recording the frequency of infection with *Amœba* without attempting a possible specific determination of the parasites.

A diagnosis of *Amœba* was made only upon finding the motile organism. All encysted forms or cellular structures resembling the vegetative form of the parasite were reported to be negative with a query, and other examinations were made until the motile organism was observed or its absence rendered reasonably certain.

The percentage of infections with *Amœba* among the 4,106 prisoners examined (23 per cent) agrees rather closely with figures previously reported by Musgrave and Clegg who found 154 (26 per cent) of 587 prisoners examined at Bilibid to have *Amœba* in the fæces.

INFECTIONS WITH INTESTINAL PROTOZOA OTHER THAN AMŒBA.

(21 per cent.)

So many atypical forms of flagellates and forms, which could not with certainty be readily placed in known genera, were encountered that the attempt to differentiate all of these organisms was abandoned at an early period and the diagnosis was made under the general term, monads. The flagellate most frequently present was *Cercomonas,* probably the usual *Cercomonas hominis* of other localities. There were three infections with *Balantidium* and three with *Lamblia.*

As in the case of *Amœba,* only the observation of the motile forms of these organisms was considered to be a safe basis for a positive diagnosis.

INFECTIONS WITH STRONGYLOIDES.

(3 per cent.)

The statistics at command for the prevalence of *Strongyloides* are the following:

Strong, 1901, Philippine Islands, 2,179 persons examined, 13, or 0.6 per cent, infected; Daniels, 1901, British Central Africa, 251 persons examined, 3, or 1.50 per cent, infected; Wellman, 1904, West Africa, 310 examined, 2 or 0.65 per cent, infected; Anæmia Commission, 1904, Porto Rico, 4,482 examined, 36, or 0.8 per cent, infected; Stiles & Garrison, 1906, United States, 3,457 examined, 8, or 0.23 per cent, infected.

Our figures (132 infections, 3 per cent) are somewhat higher than any hitherto reported. The diagnosis in every case was based upon finding the free embryo in specimens examined not more than four hours after the stool was passed.

To the best of our knowledge, hookworm ova, even in a tropical climate, never hatch in less than twelve hours after the fæces are passed.

INFECTION WITH OXYURIS.

(0.8 per cent.)

As has been repeatedly pointed out by various workers, the microscopic examination of fæces for ova is not a reliable method for the diagnosis of the pinworm, for the reason that the migration of the adult female worm to the exterior prevents such a distribution of the ova through the fæces as occurs in the case of ova which are deposited in the intestine.

The highest rate of infection with pinworms reported from microscopic examination of the fæces was that of Dobson, in India, who found 15.37 per cent of 1,249 persons to be infected; the next highest, 10.98 per cent, was reported by Grechaninoff, in St. Petersburg, in 1890, upon the microscopic examination of the fæces of 583 persons.

Some statistics based upon findings at autopsy show higher figures. Both Gribbohm and Heller encountered a fraction over 23 per cent of infection with

Oxyuris in autopsies done at Kiel, and Banik reported 30.16 per cent found in 315 autopsies at Munich. Muller, however, found only 2.21 per cent in 1,939 autopsies at Dresden and 12.13 per cent in 1,755 autopsies at Erlangen.

This parasite is directly transmissable from one person to another by means of the freshly deposited ova in the fæces, thus making it a simple matter for one person to spread the infection among those in intimate personal association with him. The chief significance of our figures for *Oxyuris* (23 cases, 0.8 per cent) probably lies in the fact that they are a favorable commentary upon the sanitary condition of the prison and also, perhaps, upon the personal cleanliness of the Filipino of the lower classes; for it might naturally be expected that when from 200 to 400 men sleep side by side in close proximity as the natives do at Bilibid, favorable conditions would arise for the spread of pinworm infection if once it was introduced.[11] Although the microscopic examination of fæces is unreliable for the diagnosis of oxyuriasis, more cases would undoubtedly have been found had there been any widespread prevalence of the infection in the prison population.

It would appear that *Oxyuris*, like *Ascaris*, tends to occur more frequently in children than in adults and (to a less degree) in women than in men, the figures compiled from different authors being as follows: Males examined, 1,543; infected, 178, or 11.54 per cent; females examined, 810; infected, 115, or 14.20 per cent; adults (over 15 years) examined, 860; infected, 39, or 4.54 per cent; children (under 15 years) examined, 1,272; infected, 305, or 23.97 per cent.[12]

Our figures (0.8 per cent) for adult males may safely be presumed to be below the percentage of infection in the total population of the Philippines.

INFECTIONS WITH TÆNIA.

(0.7 per cent.)

Rather well-defined distinctions are given between the ova of *Tænia saginata* and *Tænia solium*, but we do not consider them to be sufficiently constant and well marked to make a differential diagnosis between the two species practical from a microscopic examination of the ova alone in the general run of cases. Therefore, the distinction was not attempted unless segments of the worms were obtained. As has been shown in an earlier paper,[13] the relative number of adult specimens of *T. saginata* and *T. solium,* deposited in the Helminthological Collection of the Bureau of Science, indicated a considerably greater prevalence of the former species.

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[11] As an example of the tendency of *Oxyuris* infection to spread among persons in intimate contact, we may cite the case of a single ward in a hospital for the insane, which came under our observation in the United States. Of the 45 men in the ward, 11, or 24.44 per cent, were infected with pinworms; five other wards in the same building gave 1, 2, 0, 2, and 1 infections, respectively.

In the remaining 36 wards in other buildings (796 patients) there were only 8 infections with this parasite. *Bull. Hyg. Lab., U. S. Pub. Health & Mar.-Hosp. Serv.*, Wash. (1906), **28**, 56, 61.

[12] *Bull. Hyg. Lab., U. S. Pub. Health & Mar.-Hosp. Serv.*, Wash. (1906), **28**, 71–72.

Figures for the frequency of infection with the beef and the pork tapeworms in different localities have ranged from 0.06 to 3.66 per cent for the former and from 0.02 to 3 per cent for the latter species. Several authors have reported no infections found in large series of cases examined.[14]

INFECTIONS WITH PARAGONIMUS.

(0.4 per cent.)

The infections with lung flukes here reported were diagnosed by finding the ova in the fæces. In most of the cases they were also found in the sputum and it can not be excluded that they were present in the sputum in all cases and reached the intestines as a result of the swallowing of the eggs.[15]

Geographic distribution.—The history of the 18 patients infected with *Paragonimus* with regard to place of residence before commitment to the prison was as follows: One from Manila, one from Cavite, one from Camarines Norte, one from Albay, two from Sorsogon, four from Samar, six from Leyte, and two from Mindanao.

The central and northern provinces of Luzon were fully as well represented among the prisoners examined as were the southern provinces and the southern islands of the Archipelago, yet no patient infected with *Paragonimus* gave a history of residence north of Manila and, with the exception of the cases from Manila and Cavite, in neither of which could the possibility of previous residence in the southern provinces be eliminated, all instances of paragonimiasis gave a history of origin in the islands south of Luzon or in the peninsula forming the southern extremity of that island.

[13] *This Journal, Sec. B.*, (1907), 2, 537.

[14] *Bull. Hyg. Lab., U. S. Pub. Health & Mar.-Hosp. Serv.*, Wash. (1906) 28, 66–67.

[15] It would appear from our experience, that the value of examination of the fæces in the diagnosis of paragonimiasis has not been sufficiently emphasized, the examination of the sputum alone being usually stated as the method for diagnosis. In several cases, repeated examination of the sputum was necessary before ova could be found, although they were present almost constantly in the stools. When found in the sputum they were usually more abundant than in the fæces. If, as appears, the discharge of ova of the lung fluke in the sputum is, in some cases at least, intermittent, it is not illogical to suppose that the ova swallowed with the sputum become more or less scattered along the alimentary tract and are discharged more gradually, in less concentration, but with relatively greater constancy in the fæces. We would suggest, therefore, the value of microscopic examination of the fæces as well as of the sputum in the diagnosis of lung-fluke infection.

Therefore, the conclusion would appear to be warranted that infection with lung flukes is not evenly distributed throughout the Philippines, as appears to be the case with the parasites above considered, but that it is to be found chiefly in the southern portions of the Archipelago.

It is quite within the bounds of probability that the distribution of this parasite may be found to be even more strictly localized. To the best of our knowledge, all cases of paragonimiasis reported for the Philippines, in which the history of previous residence was known, have originated in the southern part of the Islands, and further investigation may show the infection to be *confined* to this region. The possibility can not be excluded that the infection is limited more or less strictly to certain of these southern islands. Some indication of this was found in our own figures. For instance, 239 prisoners from the Island of Leyte were examined and 6 had paragonimiasis; 127 prisoners from the Island of Samar gave four infections with lung flukes; on the other hand, while 248 prisoners from Panay were examined, no fluke infections occurred. However, until the matter has been further investigated, we believe that the only generalization justified by our results is as already stated: namely, that paragonimiasis prevails in the southern rather than in the northern parts of the Philippines.

INFECTIONS WITH SCHISTOSOMA JAPONICUM.

(0.6 per cent.)

The use of the specific name seems desirable in the present case in order to differentiate *Schistosoma japonicum* from *S. hæmatobium,* all of our infections being with the former species.

Geographical distribution.—As in the case of *Paragonimus,* the apparently uneven geographical distribution of *Schistosoma* infections appears to be of greater interest and importance than the actual percentage of infection found among the prisoners examined. The cases of schistosomiasis were distributed geographically as follows: Manila, 1; Samar, 6; Leyte, 5; and Mindanao, 4. Therefore, excepting the one case from Manila, all infections with *Schistosoma* appear to have originated on the three southern islands, Samar, Leyte, and Mindanao.

INFECTIONS WITH OPISTHORCHIS.

(0.3 per cent.)

Racial and geographical distribution.—In only five of the eleven cases of opisthorchiasis could a definite history of previous residence be obtained. Three of these came from the Island of Mindanao, one from

Rizal Province, Luzon, and one from Nagasaki, Japan. Five of the prisoners having *Opisthorchis* infections were Chinese, five were Filipinos, and one was Japanese.

The results for *Opisthorchis* are not sufficiently complete to show any marked inequality of distribution among different localities. However, there does appear a relatively greater prevalence of this parasite among the Chinese. In one case it was certain that the infection was contracted in China, but in the other instances this point could not definitely be determined.

INFECTIONS WITH HYMENOLEPIS.

(0.1 per cent.)

Four of the five infections with *Hymenolepis* were with the "dwarf tapeworm" of man, *H. nana;* the remaining one was with *H. diminuta.*

Statistics by several authors show that the dwarf tapeworm is consistently more common among children than among adults, and therefore we would expect our figures to be somewhat higher for this parasite had children been included among the cases examined.

DISCUSSION.

The purpose of the investigation, as was stated in the introduction, was to obtain accurate knowledge of the prevalence and distribution of animal parasites among the Filipinos so as to secure more definite judgment regarding the importance of animal parasites as factors in determining the hygienic and industrial condition of the people, and to obtain a clearer idea in regard to the nature and magnitude of the medical and sanitary problems presented and, perhaps, also to make some contribution toward their solution.

The results of this investigation show one of the most striking instances in the history of medicine of a population almost universally infested with animal parasites; and the medical and sanitary problems presented would seem to offer three rather distinct aspects, namely, the infections with intestinal protozoa, chiefly *Amœba,* the trematode infections, and the infections with intestinal worms.

The situation in the Philippines in regard to amœbiasis is involved in differences of opinion both as to the specific identity of *Amœba* found in the intestine and to their pathogenicity. Whether or no the validity of Schaudinn's *Entamœba histolytica* and *E. coli* and the nonpathogenic nature claimed for the latter species be ultimately established, we are forced to believe, as we have already indicated, that in our present state of knowledge the only safe position for the medical man to hold in the Philippines toward amœbic infections is to consider all intestinal *Amœba* as potentially pathogenic.[15]

Accepting such a view, our figures would appear to prove from a statistical view point the wide prevalence of amœbiasis already recognized by clinicians and to emphasize the extreme value of the prophylactic measures urged by the Bureau of Health and the great need of rapidly extending sanitary measures against this parasite. The magnitude of the problem appears when we consider that if our figures for the Bilibid prisoners (23 per cent) be applied to the total population of the Islands, from 1,500,000 to 2,000,000 people in the Philippine Islands harbor intestinal *Amœba.*

The unsolved biological problems in connection with *Paragonimus, Schistosoma* and *Opisthorchis,* involving their embryonic development, and intermediate hosts and modes of infection, leave us only general measures of treatment and of prophylaxis in these infections. The apparent localization of *Paragonimus* and *Schistosoma* in the southern part of the Islands renders our figures of little statistical value, and further work in the localities in question will be necessary in order to determine their actual frequency of infection in infected localities.

The situation in the Philippines in regard to the prevalence of intestinal worms calls for special consideration because of the high rate of infection found, the peculiar character of the hookworm situation, and because these infections are apt to be lightly regarded in the tropics.

The prisoners at Bilibid showed an average of 142 infections with intestinal worms for each 100 examined. Fifty-two per cent were infected with hookworms, but it would appear that these parasites do not produce the serious effects in the Filipino that they do in other races; hence, they should be placed in the same category with other intestinal worms.

While it is generally recognized that verminous infections of the intestine are indirectly and in an indefinite degree injurious, it is extremely difficult to obtain and it is practically impossible to demonstrate any accurate measure of the injury done. So far as we are aware, the work which by its results has come nearest to demonstrating the effects of infections with intestinal worms upon the health of a population is that carried on by Dr. Shattuck of the Bureau of Health at Bilibid Prison during the time our own investigation was in progress, the results of the same examinations being used as far as practicable in both investigations.

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[15] It would not be within the purpose of the present paper to enter into a discussion of the merits of the questions regarding the specific identity and relative pathogenicity of intestinal *Amœba.* If all intestinal *Amœba* are pathogenic, it is a rather startling condition of affairs to find 23 per cent of a population harboring this parasite; but it would appear that such a view is rather in harmony than otherwise with the frequency of amœbic lesions found at autopsy. In this connection, the reader is referred to earlier publications of Musgrave and Clegg in the Philippine Journal of Science, and to Gilman's report upon a series of 100 autopsies at the Philippine Medical School which appears in the current number.

These results have been placed at our disposal by Dr. Heiser, Director of Health, from the manuscript of his Annual Report for 1906–7, and are briefly as follows:

The annual death rate in the prison when it came in charge of the Bureau of Health was 238 per one thousand. The institution of general measures of sanitation reduced this rate to 75 per one thousand where it remained stationary, resisting further reduction. Up to this time little attention had been paid to infection with intestinal worms. In the latter part of 1906, systematic treatment of the prisoners for intestinal worms was begun and vigorously carried out until practically the entire population of the prison had been treated. Following, and, in Dr. Heiser's opinion, largely as the result of this antihelminthic campaign among the prisoners, the death rate dropped to 13 per one thousand per annum.

Whether or not this apparent relationship between intestinal worms and the death rate at Bilibid will be substantiated by future records at the Prison, or would be confirmed by the institution of a similar campaign throughout the Islands, its significance can scarcely be overestimated even though ultimately the results should prove to be but a fraction of what was apparently accomplished among the Bilibid prisoners. It moreover sharply emphasizes the fact that the absence of direct, acute manifestations of intestinal helminthiasis should not blind us to the vital importance of these infections as factors in determining the hygienic condition of a people.

Applying the rates of infection obtained from the 4,106 prisoners examined at Bilibid to the total population of the Islands (about 7,000,000), it would appear that about 5,000,000 persons in the Philippines are infected with intestinal worms and that the inhabitants of the Islands harbor over 9,000,000 infections. The magnitude of these figures indicates in part the tremendous proportions of the problems involved in any radical movement toward improvement of existing conditions, especially when we consider that the situation does not appear to be simplified by any marked confinement of the infections to limited areas. Even a casual knowledge of sanitary conditions prevailing throughout the Islands throws additional light upon the difficulties to be encountered and leads to the question whether it is practicable at the present time to institute special prophylactic measures directed toward the eradication of intestinal worms, or whether we must content ourselves with the gradual sanitary improvement of the country.

In this connection, one practical suggestion would seem to offer itself. The source of all infections with intestinal worms, followed back to its origin, is necessarily the fæces of persons already infected.[16] With this fact in mind, we have carefully inquired into the different methods of the disposal of excreta customary among the Filipino people and it would appear that it would scarcely be possible to establish more ideal conditions for the spreading of intestinal parasites throughout the Islands. The native, if living near a stream, defecates along its banks, either in, or at varying distances from the water; in the rainy season, the streams overflow their banks and naturally scatter any infection they carry over the adjacent country. Another manner of disposing of the fæces, equally or perhaps more prevalent, is simply through a hole in the floor of the bamboo house, the excreta falling to the ground to be partly devoured and partly scattered about by the universally present hogs and chickens.

Such conditions go together with the extremely high prevalence of intestinal worms among the people, and we can scarcely escape the conclusion that the one sanitary measure preëminently demanded for the prevention of infection with intestinal worms in the Philippines is a proper disposal of human excreta. In fact it would appear scarcely too strong a statement to say that the spread of infections with intestinal worms could be in time satisfactorily controlled by the proper establishment of this measure alone. The urgency of the demand for a proper disposal of human excreta is further emphasized by the effect which it might reasonably be expected to bear directly upon the prevalence of other diseases, in that it would lessen the distribution of pathogenic organisms other than animal parasites which escape in the fæces.

To devise a working system, practical, economical, and adapted to Philippine conditions, is a special problem which requires special and, perhaps, experimental study. That a radical sanitary measure can be effectively and promptly enforced in the Philippines has been strikingly exemplified by the campaign of vaccination against smallpox so successfully carried out by the Bureau of Health.

In conclusion, we believe that the most valuable practical lesson to be drawn from the results of the examination of the Bilibid prisoners is the imperative need of establishing throughout the Philippines a system for the proper disposal of human excreta. Moreover, it does not seem unreasonable to expect, in the light of the striking results apparently accomplished at Bilibid by treating infections with intestinal worms, that with the reduction in the present exceedingly high prevalence of intestinal worms in the population, the general hygienic condition of the people would be improved to such a degree that there would follow a material reduction in the present high rates of morbidity and of mortality from tuberculosis and other prevailing diseases.[17]

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[16] Those cases in which the parasite may infect other animals as well as man would, of course, constitute rare exceptions to this statement: for example, *Hymenolepsis* in rats, *Tænia solium* in hogs.

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[17] The following resolution was unanimously adopted at the recent annual meeting of the Philippine Islands Medical Association, held at Manila, February, 1908:

"Whereas, it would appear that the rate of infection with intestinal worms is higher among the Filipinos than has ever been definitely reported for any other people; and

"Whereas, it would appear further that the death rate at Bilibid Prison has been materially reduced following the treatment of the prisoners for these infections; and

"Whereas the spread of infection with intestinal worms can be controlled almost absolutely by the proper disposal of human excreta; and

"Whereas, the proper disposal of human excreta would, at the same time, remove one of the most dangerous channels for the dissemination of other infectious diseases: Therefore, be it

"*Resolved*, That the Philippine Islands Medical Association does petition the Government of the Philippine Islands, through the honorable the Secretary of the Interior, that a commission of five properly qualified members be appointed to decide upon the most practical and efficient methods for the disposal of human excreta that can be established in these Islands and that such appropriation be made and such means provided in accordance with the report of this commission as may be necessary to put into effect a practical and expedient working system for the disposal of human excreta."

A REPORT ON THE FIRST ONE HUNDRED AUTOPSIES AT THE·PHILIPPINE MEDICAL SCHOOL.

By PHILIP K. GILMAN.

(From the Department of Pathology and Bacteriology, Philippine Medical School.)

There have been a large number of autopsies performed by the Bureau of Government Laboratories and its successor, the Bureau of Science since the American occupation of these Islands. While in the cases of acute infectious diseases the diagnoses have been carefully made and recorded, and in other special cases full protocols have been preserved, in general the records are not adapted to furnish the basis for a complete statistical study of the relative frequency with which the different chronic diseases occur. A systematic study has been made, by gross and histologic methods, of the pathologic material, and complete records of the findings have been kept since the opening of the Philippine Medical School, in the department of pathology and bacteriology organized by Dr. H. T. Marshall. The examinations are made according to the usual Virchow routine, and are designed especially to furnish material and records for a general statistical inquiry. The routine includes the preservation of pieces of the organs in Zenker's fluid and subsequent histologic examinations.

No unusual efforts have been made to discover remote foci of tuberculosis or syphilis, and the examination for the presence of intestinal parasites has not been altogether complete. Cultures were made in only a few instances. The nerves were examined for degenerations in only one or two cases in which a clinical report rendered the diagnosis of beriberi probable.

The following report is based upon the findings in the first one hundred autopsies performed at the Philippine Medical School between August, 1907, and January, 1908. Although the number of cases is comparatively small, these findings should give a good conception of the relative frequency among the lower classes of Filipinos of the commoner diseases, with the exception of the acute epidemic ones, for the bodies came from the free wards of the large hospitals and from the poorer quarters of the city of Manila. Cholera, smallpox, leprosy, etc., are treated only in the special hospital for these diseases, and such conditions would not enter into our records except on rare occasions.

Of the 100 bodies examined, 67 were males and 33 females, 97 being Filipinos and 3 Japanese. As is shown in the following table, the third and fourth decades contributed the greatest number of cases, these two furnishing nearly equal numbers:

Decade.	Male.	Female.	Total.	Decade.	Male.	Female.	Total.
1	7	7	14	6	7	2	9
2	5	5	10	7	4		4
3	17	6	23	8	3	2	5
4	15	6	21	9	1	2	3
5	8	2	10	10		1	1

Tuberculosis was found to be the cause of death in 35 of the cases; pneumonia in 27; chronic cardiac disease and arterial change in 6; nephritis in 5; typhoid fever, beriberi, and septicæmia each in 4; amœbic dysentery and acute bacillary dysentery each in 3; acute endocarditis in 1; carcinoma in 2; and acute pleurisy, acute peritonitis, splenomegaly, cerebral abscess, cerebellar hæmorrhage, and acute yellow atrophy each in 1 case.

TUBERCULOSIS.

Tuberculous lesions were found forty-five times in the series of 100 cases and tuberculosis was the cause of death thirty-five times; 22 of these cases were males and 8 females. The autopsy on the youngest person was of a child 1 year old, on the oldest, of a man of 90 years. The greatest number of cases, 18, occurred between the ages of 25 and 35, the next greatest, 12, between the ages of 45 and 55 years.

The disease was confined to the thorax in 21 cases, to the lungs and alimentary tract in 6, to the lungs and kidneys in 2, to the peritoneum in 4, and was a generalized process in 2. Nearly an equal number of the cases occurred in people who had lived in the country and in those coming from the city of Manila proper, in both of which situations the elevation of the land is very little above that of the sea level.

The large amount of lung tissue involved was of particular interest in the cases of pulmonary tuberculosis. In six instances the greater part of all the lobes of both lungs was thickly studded with lesions. Complete, massive involvement of both upper lobes occurred in 7, one entire lung and at least one lobe of the opposite lung were involved in 2, the entire upper right lobe in 3, and the left in 2 cases. The left upper lobe was diseased in 26, the right upper lobe in 23 cases.

The type of tuberculous lesion most frequently met with consisted of a chronic ulcerated condition in which ragged, irregular cavities, frequently of great size, connected with one another and with bronchi. This condition was found to a greater or less degree twenty-seven times, or in about 90 per cent of the cases of pulmonary involvement.

Histologically, the irregular, ragged walls of these cavities were in the majority of instances not definitely limited by any marked reaction on the part of the surrounding lung tissue. A definite formation of new fibrous tissue was found in but one-third of the cases and this zone was nearly always lined with a layer of newly formed tuberculous tissue.

Extensive areas of consolidation were frequently found associated with the cavity formation, and in a contiguous portion or adjoining lobe great showers of miliary and conglomerate tubercles were encountered.

The pleura was involved in all cases, the involvement consisting in a chronic, fibrous thickening and obliteration of the cavity which varied from a localized area to complete union of the surfaces. In addition to the cases of tuberculosis, pleural lesions were found very frequently, 50 per cent of the cases included in this report showing some pleural involvement.

Tuberculous peritonitis was the cause of death in four cases. One of these showed a small, active focus of the disease in the lungs, one an apparently healed apical lesion, and after a prolonged search the other two revealed no pulmonary involvement. Tuberculosis of the vertebræ occurred but once and of the bladder three times; psoas abscess was also present once. Latent tubercular lesions were found in the lungs in but 2 of the 100 cases, and healed foci occurred in but 6.

In connection with this evidence of the virulence of the tubercle bacillus, it is interesting to note that cultures of the organism obtained by subcutaneous inoculation of guinea pigs and subsequent transference from their glands to suitable media, were kept alive with considerable difficulty and soon died out after a very sparse growth.

PNEUMONIA.

Pneumonia was the cause of death in 27 cases, 11 of these being croupous or lobar, and 16 broncho-pneumonia, the majority of the cases occurring in young adults and three-fourths coming from the city proper. A summary of the cases of lobar pneumonia shows that all lobes of both lungs were involved in 1 case, the entire right lung in 1, the left lower lobe in 5, the remaining 4 cases showing involvement of but one lobe. All were accompanied by an exudation of a fibrinous nature upon the pleural surface of the involved lung.

Death in this series of 11 cases occurred early in the disease in four instances, and during the stage of red hepatization in two instances. In the former, the tissue involved was in an early stage of engorgement with greatly distended capillaries and swollen epithelium surrounding but a small number of red corpuscles. The remaining five cases showed typical, gray hepatization.

Unresolved pneumonia was found in one case, with typical fibroid induration of the entire lobe. The patient died of an acute beriberi.

The following complications of pneumonia were presented: endocarditis in 2 cases, pericarditis in 1, nephritis in 5, and pleurisy in all but 2 of the early cases.

Primary broncho-pneumonia occurred in 3 of the 15 cases of this disease, all of these being in children of 3 years of age. Seven cases of the secondary form of disease had developed during the course of infectious diseases and 5 were in old, emaciated subjects and were of the aspiration or deglutition type.

Other pulmonary lesions were encountered in the routine examination of the organs from autopsies, as follows: œdema and congestion in 27 cases, infarction in 5, and emphysema in but 2 cases.

HEART AND BLOOD VESSELS.

Death could be ascribed to chronic cardiac change associated with arterial degeneration in but 6 of the 100 cases, but it is also true that a normal heart was the exception, some change in or within the walls occurring in 62 instances. In 4 of the above-mentioned 6 cases, an acute dilatation of an hypertrophied organ was found associated with more or less rigid curling of the mitral valves and damage to the lining of the aorta; in the other two cases, there was a marked grade of fatty infiltration, the muscle fibers being completely occupied with rows of small globules. Stenosis was observed but once, the mitral orifice being affected.

The common type of heart found in the majority of instances was a flabby, relaxed, more or less dilated organ, showing practically no attempt at hypertrophy. The heart muscle in these cases was pale brownish or yellowish-brown in color, possessed a turbid appearance and was very soft. Histologically, the fibers showed varying grades of granular degeneration. Fragmentation was frequently observed and in the greater number of the specimens studied very little new formation of scar tissue had occurred. A condition of relative insufficiency was found in 26 cases.

Acute disease of the endocardium followed an operation for imperforate anus in a child of 5 days, and occurred as a complication of pneumonia twice. In each of the cases there was a vegetative inflammation of the mitral valves.

Acute myocarditis was present in five instances, four in cases of beriberi and one in acute yellow atrophy of the liver. Acute pericarditis occurred once in a child of 1 year and 8 months, who died of broncho-pneumonia.

Arterial changes were the exception in this series of examinations. The vessels in only 6 of the 100 bodies showed thickening and loss of elasticity and of the 6, but 2 evidenced a marked grade of degeneration with scattered plates of calcification confined to the abdominal aorta. The other 4 showed numerous flat, yellowish, oval projections scattered over the surface of the aorta near its origin. No change more marked than a partial loss of elasticity was encountered in the vessel walls, even in cases over 60 years of age. Arterio-sclerosis was found in but one of the 25 individuals infected with tuberculosis.

Aneurism was not encountered in any of the series, nor has a case been admitted in the hospital wards or been seen among the patients of the large free clinic at St. Paul's Hospital during the past eight months.

DISEASES OF THE KIDNEYS.

Lesions of the kidneys occurred more frequently than one might expect from the generally good condition of the arterial tissue. Of 100 cases, nephritis was present in 48, acute in 23 and chronic in 25. Retention cysts occurred in 7, infarcts in 2, and tuberculous foci in 4 cases.

The kidneys usually appeared swollen and markedly congested in the instances of acute nephritis, the capsule stripping readily and leaving a dark, smoky surface. Histologically, the glomerular changes predominated, the capsules and tubules frequently containing red and a few white blood cells. The swelling and granular appearance of the tubular epithelium was in most instances less marked than the glomerular change.

The kidneys with chronic nephritic changes were of the large, pale type in 6, and the small granular in 19 cases. Two cases of the first group showed large, pale, swollen organs with numerous opaque areas scattered over the smooth surface beneath the capsule; the pale cortex forming a sharp contrast to the darkly injected pyramids. Histologically, the tubules, glomeruli, and interstitial tissue were all more or less involved in the imflammatory process. The four other cases of this group evidenced somewhat small, pale kidneys with thickened capsules and roughened surfaces. Glomerular degeneration and a rather marked grade of of interstitial change was present, hyaline changes being frequent.

Contracted, roughened kidneys with firmly adherent capsules were found in seven instances in the remaining nineteen cases of chronic nephritis. The capsules covered small cysts. This type of kidney could only be cut with increased resistance; it showed an attenuated cortex which contained a greatly increased amount of interstitial tissue, with marked degenerative and atrophic changes in the glomeruli and plugging of distorted tubules with débris. The arterial change in these cases of chronic nephritis is less marked than the general change in the organs would lead one to expect, with the exception of those cases in which there was a general arterio-sclerosis.

Fatty degeneration of the kidney was found in 4 cases, 3 of which died of tuberculosis and 1 of amœbic dysentery.

The suprarenal bodies were tuberculous in two instances, both of which contained, in addition, marked pulmonary lesions.

SEPTICÆMIA.

Death from a septicæmia advancing from local infection occurred in 4 cases. The post-partum uterus served as the point of entrance in 1 instance, in 2 the foci resulted from compound fractures, and in the fourth, a small pustule on the lower lip was the beginning of the infection. It is of interest to note that in none of these cases was a streptococcus demonstrated. *Staphylococcus aureus* and *albus* and *Bacillus pyocyaneus* were obtained from the body in which infection had taken place from the lip and also from the puerperal case. Judging from the difficulty experienced in endeavoring to obtain a culture of the *Streptococcus pyogenes* for class work in the Medical School, this organism does not play as important a rôle in the Philippines as it does in other parts of the world.

LESIONS OF THE ALIMENTARY CANAL.

The condition of the teeth in this series was bad. Black, discolored cavites and decayed areas were frequent. The gums were irregular and receding and pyorrhœa alveolaris was common.

Disease of the hard palate, a perforation probably of a syphilitic nature, occurred in one case.

Chronic ulceration of the stomach occurred once, the punched-out ulcer with irregular edges lying on the greater curvature, 5 centimeters from the cardiac orifice. An acute hæmorrhagic inflammation of the mucosa of the stomach occurred in two cases, dead of beriberi.

One instance of malignant disease of the stomach was encountered. The tumor, an adeno-carcinoma, infiltrated the lesser curvature of the organ from the cardiac orifice to within 3 centimeters of the pylorus. The surface of the tumor within the stomach was ulcerated and surrounded by a rolled, irregular edge. The stomach was adherent to the pancreas and the under surface of the liver, the latter being infiltrated with scattered metastatic growths.

Two of the cases of pneumonia and one of chronic Bright's disease showed an acute colitis with a thin layer of exudate on a markedly congested base. In one case of acute nephritis, the solitary follicles of the ileum were enlarged and many were topped with areas of necrosis. Ulceration in the ileum was present in all of the cases of typhoid fever.

One hundred appendices were examined: 19 were over 12 centimeters in length, 6 showed a chronic obliterative process, 7 contained fæcal masses and adhesions were present four times. The appendix in 24 cases was found to extend dorsally around the end of the cæcum and up between the cæcum and the parietal peritoneum.

Death from acute bacillary dysentery occurred in three cases. Two of these were in Japanese brothers, aged 2 and 4 years, dying the same day.

The lesions most frequently met with in the entire series of cases were ulcerations of the large bowel. The lining of the large intestine in 32 cases showed active amœbic ulcerations of typical appearance, while in 22 additional individuals there were abundant evidences of previous lesions as shown by numerous, irregular pigmented scars and depressions. While these lesions were spread generally over the entire extent of membrane from the ileo-cæcal valve to the rectum, in 11 cases the ulcerations were confined to the terminal few centimeters of the rectum.

Intestinal worms were found in 32 cases, *Ascaris lumbricordes* alone in 17, *Trichocephalus dispar* in 7, and the two together in 8. A liver fluke, *Opisthorchis sinensis,* was encountered in one body.

A persistent Meckel's diverticulum was present in a female child, dead of pneumonia, and an imperforate anus in a male child.

LESIONS OF THE LIVER.

Only one case of abscess of the liver occurred in the series. The body was that of a Japanese aged 36, in whom the entire large bowel was lined with amœbic ulcerations. The abscess occupied the lateral portion of the right lobe of the liver and measured 10 centimeters in diameter. The cavity was limited above by the diaphragm and contained a thick, yellow-brown pus. Numerous amœbæ appeared in the sections of the wall of the cavity.

The livers from 2 cases of typhoid fever, 1 of broncho-pneumonia, and 2 of pulmonary tuberculosis, showed well-marked areas of focal necrosis, in addition to a general parenchymatous degeneration. In 38 cases the same organ evidenced chronic passive congestion. The enlarged, dark red, firm organ was more frequent than the so-called "nutmeg" liver. The majority of the 38 cases were those of patients dead of pulmonary tuberculosis, and in addition they showed degenerative changes in the myocardium.

A mild grade of fatty infiltration was demonstrated in 17 of the livers from cases of tuberculosis and a very marked grade in 4 additional instances, 2 of tuberculosis, 1 of amœbic dysentery, and 1 of chronic heart disease. The general picture in the series of sections of fatty livers was of large fat-droplets occupying the greater part of an entire cell and often causing complete disappearance of the cell plasm.

Amyloid occurred in the livers in two of the tuberculous cases.

In nine cases the liver was the seat of cirrhotic changes. The organ was generally enlarged and firm. Three of the cases had fluid in considerable amount in the peritoneal cavity. The new tissue throughout the liver substance was rather closely confined to the periphery of the lobules, often inclosing groups of several lobules, the inclosed cells showing atrophy. Of the 9 cases, 5 died of pulmonary tuberculosis, and 1 of peritoneal tuberculosis. No marked "hobnailed" liver was found. Acute, yellow atrophy of the liver occurred in one case, that of a woman 20 years old in the fifth month of pregnancy. The liver measured 18 by 5 centimeters; the edge was rounded, the organ was soft and of an opaque, grayish-yellow, mottled color. The organ was largely made up of degenerated and necrotic cells, irregular collections of fat-droplets and detritus.

There was but one instance of neoplasm of the liver, which occurred in the case of gastric carcinoma; the liver showed numerous metastases distributed throughout its substance.

PERITONEUM.

The single case of acute peritonitis followed a stab wound in which an opening into the descending colon had occurred.

In four cases, in addition to those of ascites associated with cirrhosis of the liver, there was a large amount of peritoneal effusion. One of these was associated with splenomegaly, two with cardiac failure, and one with nephritis.

LESIONS OF THE SPLEEN.

An acute swelling of the spleen was found in ten instances, in cases of typhoid fever, septicæmia and pneumonia. A chronic enlargement of this organ was encountered in sixteen instances, its enlarged condition apparently having no direct connection with the disease causing death. A chronic, indurative splenitis with a diffuse extensive formation of connective tissue was the rule in these specimens. The capsule, more or less thickened, had lost its smooth surface and was not infrequently ridged and seared. The organ was firm, although not hard, and usually increased in size and weight.

The cut surface of this type of spleen was of a uniform, red-brown color and crossed in all directions by a prominent interlacing framework of connective tissue. As a rule, the Malpighian bodies could not readily be distinguished. Microscopically, the finer connective tissue framework was increased or thickened and there was generally an increase in the number of parenchyma cells. Pigmentation was uncommon. It was observed four or five times and then the areas were made up of extremely fine, brown-black granules.

An atrophied spleen, wrinkled and firm, with prominent Malpighian bodies and decreased parenchyma, occurred in four cases, of which three were in patients who had lived to over 80 years, the other being an emaciated woman of 45, dead of carcinoma. The spleen in the series of cases of tuberculosis was the seat of tuberculous foci in two instances.

A single case of splenomegaly was encountered. The spleen weighed 1.2 kilos. The body was that of a well-nourished laborer 33 years old; the peritoneal cavity contained 2 liters of pale, turbid fluid, although there was no cirrhosis of the liver. The enlarged spleen was attached by œdematous adhesions to the former organ, the stomach, kidney and bowel. The thymus and lymphatic glands were not enlarged. There were eleven smaller accessory spleens, measuring from 0.5 to 1.8 centimeters in diameter, extending in an irregular chain along the tail of the pancreas from the hilum of the main organ to the mid-line of the body. The accessory organs showed a shrinkage of the Malpighian areas and proliferation of the endothelial lining of the cavernous spaces in common with the main organ.

In addition to the above case, accessory spleens were encountered in three other subjects.

LYMPHATIC SYSTEM.

The bronchial lymph glands were involved in 27 of the tuberculous cases. A general involvement of the mediastinal glands also occurred in 3 cases. The bronchial glands were diseased twice in company with the mesenteric, and in 3 other cases the latter showed a general involvement alone.

The glands of the axilla were enlarged in but one instance in the entire series of cases. The glands of the groin, on the other hand, were found as a rule to be somewhat enlarged and firm. Histologically, they showed an increased growth of reticular tissue. Old scars, proving previous abscess formation in the glands of the groin, were found in two cases. In none of the glands could signs of syphilitic induration and cell change be detected, and in but one case was there evidence of a primary syphilitic lesion. In this instance there was a perforation of the hard palate.[1]

NEOPLASM.

Carcinoma as a cause of death was found twice, once involving the stomach, and once the cheek and antrum. There is a belief prevalent among some medical men that malignant disease is rare in this part of the world, but if reference be made to records of the department of surgical pathology this is shown not to be the case. Of 100 specimens sent from the surgical clinic at St. Paul's for routine examination, 6 were malignant, 4 sarcomata, and 2 carcinomata. The sarcomata were all of periosteal origin and of the lower limb.

There was one case of dermoid cyst of the ovary among the autopsies, the tumor measuring 14 centimeters in diameter. It contained several areas of calcification, in addition to the usual cuticular structures.

Uterine myomata—all subserous—were found in 3 cases.

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[1] This case was clinically considered one of gangosa.

THRYOID GLAND.

The only case of disease of this gland was one of general symmetrical enlargement occurring in a woman who had suffered from tuberculosis. Colloid formation was the principal change associated with several small cysts. The thryoid glands were otherwise quite small, often showing irregular lobulations. No instances of accessory thryoids were encountered.

NERVOUS SYSTEM.

Degeneration of the vagus and phrenic nerves were demonstrated in one case of beriberi which caused death in an infant of 3 months.[2]

Lesions of the central nervous system included one case of cerebellar abscess following otitis media, one of cerebral softening and one of hæmorrhage following an occipital fracture.

The meningeal coverings of the two cerebral hemispheres in a case of arterio-sclerosis were adherent and thickened, and inclosed numerous small collections of clear fluid in cyst-like, flattened spaces within the opaque membranes. Microscopically, this thickened layer of adherent membrane showed a richly interlacing meshwork of fibers, in the spaces of which there were many large polyhedral cells with large, deeply staining nuclei and granular protoplasm. The blood supply was poor, the walls of the vessels showing an advanced grade of atheroma.

No gross syphilitic disturbances of the central nervous system were encountered.

GENITALIA.

Disease of the male generative system was uncommon. There was one case of scrotal and one of prostatic abscess. Three cases of hydrocele on the left side were encountered. Tubercular cystitis occurred in three cases, nontubercular in one.

SKIN.

The cutaneous lesions included 1 case of *Impetigo contagiosa*, 1 of leucoderma, and 4 of chronic ulceration. The ulcers in 3 cases were confined to the ventral aspect of the leg and in the fourth an ulcer 4 centimeters in diameter was present on the dorsal surface of the right elbow.

One case of supernumerary thumb was seen. The two thumbs were of equal size, each 1 centimeter shorter and smaller in proportion than the normal thumb on the left hand. They formed a Y-shaped junction at their union, being articulated side by side, with separate surfaces at the end of each of the two metacarpals. Each thumb was well formed and bore a perfect nail.

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[2] This case was reported by Dr. Albert at the Fifth Annual Meeting of the Philippine Islands Medical Association, Manila, February 26–29, 1908.

SUMMARY.

A summary of the findings in these cases brings out certain points, some of which at least are of particular interest. Some idea of the importance of tuberculosis as a cause of death in these Islands is shown by the number of cases in this series, 35 per cent, and an idea of the virulence of the disease when once established may be drawn by comparing these figures with the number of cases showing healed tuberculous foci, 6 per cent, and latent foci, 2 per cent. The disease as encountered here is a rapidly progressing one, and the amount of tissue destroyed and thrown out of function is marked.

The frequency of chronic degenerative change of the myocardium and of nephritis is more noticeable when compared with the relatively small number of cases of arterial degeneration. The number of ulcerations of the large bowel, 32 per cent, and scarring, 22 per cent, while large, is smaller than the percentage of cases found by Musgrave in his series of examinations.

A feature by no means the least interesting is the absence of syphilitic lesion in all but one case.

NOTES ON THE CONDITION OF THE LIVER IN SCHISTOSOMIASIS.[1]

By J. M. PHALEN and HENRY J. NICHOLS.[2]

I. INTRODUCTION.
II. CASE RECORD.
III. PATHOGENESIS OF THE CIRRHOSIS OF THE LIVER.
IV. COMPARISON OF INFECTION WITH SCHISTOSOMUM JAPONICUM AND SCHISTOSOMUM HÆMATOBIUM.
V. GEOGRAPHICAL LOCATION.

I. INTRODUCTION.

Schistosomum japonicum was discovered and described as recently as 1904, although the disease which it produces had been recognized in Japan for nearly two decades previously. Outside of a small area in Japan, cases of infection with this blood fluke are still so infrequently seen that each one is worthly of report and discussion, as such reports will aid in locating the geographical distribution of the parasite and in clearing up its life history and pathologic effects. In discussing the present case, we wish to speak particularly of the pathologic findings in it and in other recorded cases, and to draw a contrast between these and those of infection with the closely allied *Schistosomum hæmatobium*.

II. CASE RECORD.

The patient, P. O., was admitted on January 16, 1908, to Dr. Ruffner's service in the Division Hospital in this city, and died on the following morning. He was a Filipino soldier 30 years old, belonging to a Visayan Scout company, single, and a native of Calbayog, Samar, in which town he lived continuously until his twenty-fourth year. He then enlisted and during the six years of his service was stationed on the Islands of Panay, Cebu, Leyte and Samar. He had never been out of the Visayas except for short visits, and he was on furlough in Manila when he entered the Division Hospital. The sick record of his company shows that during the six years of his service he was in hospital one hundred and nineteen days and in quarters eighty-three days, although the causes of admission to sick report are not given.

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[1] Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, Manila, February 27, 1908.

[2] Captain, Medical Corps, United States Army, and first lieutenant, Medical Corps, United States Army, constituting the United States Army Board for the Study of Tropical Diseases, as they occur in the Philippine Islands.

When he was admitted to the Division Hospital he was suffering from diarrhœa and cramps. His heart action was weak, rapid and irregular, and a diagnosis of myocarditis, probably due to beriberi, was made.

Autopsy by Dr. Whitmore three hours after death of the patient. The body is well developed and well nourished and, with the exceptions hereafter noted, the organs present no macroscopical alterations. Upon opening the abdomen, the *liver* and *spleen* are found to be moderately enlarged, the latter being somewhat adherent. The liver is not cirrhotic in appearance, but presents pale patches over its surface, and, more particularly, many whitish nodules varying in size up to the head of a pin, and situated under the capsule. On excising and crushing these nodules, oval eggs are found measuring approximately 70 by 40 μ. On section, many more nodules are seen scattered throughout the entire organ. The small intestines harbor a small number of hookworms; they present no gross changes, while the large intestine shows only one small area situated low down in the bowel, where the mucous membrane is swollen and injected. The bowel contents show ova similar to those in the liver, but these are few in number, and ova of uncinaria are also present.

Histologic examination.—Tissues were secured from the liver, kidneys, lungs and intestines. These were preserved in Kaiserling's solution and in formalin, imbedded in paraffin, sectioned and stained with hæmatoxylin and eosin and with Bismarck brown and eosin. A microscopic study of the liver shows the presence of ova either in groups or singly, usually occurring in the interlobular connective tissue (Pl. I, fig. 1), but also occasionally throughout the parenchyma, and in one instance an ovum is found apparently lodged in the intralobular vein. There is a considerable increase in the connective tissue around the lobules and encroaching upon them. The staining of the tissue is irregular, being quite faint in places.

The most striking feature is the presence of the miliary nodules noted above. (Pl. I, fig. 2.) These tubercular-like nodules are mentioned by Katsurada, but are said to occur rarely in the parenchyma. Our sections show them situated exclusively in the parenchyma occupying the place of a lobule or of two or more lobules fused together. The central area stains deepest, and is composed of an indefinite mass of nuclei, red blood cells and fibrin. It is quite sharply defined from the next zone which is made up of young connective tissue radiating toward the center. This zone gradually merges with a ring of still younger connective tissue belonging to the interlobular tissues. Some nodules have a small center and are evidently being gradually walled off and replaced by new connective tissue growth beginning at their peripheries. Throughout this connective tissue there is a new formation of bile channels, apparently an effort to repair the damage to the lobule. Ova are usually present in small numbers in these nodules. (Pl. I, fig. 3.)

Sections of the large intestine show the presence of ova in small numbers in the submucosa, accompanied by a moderate increase in the connective tissue. They occur in small groups outside the vessels close to the *muscularis mucosæ*. Ova are also found in the mucosa lying close to the epithelial cells of the glands of Lieberkühn. The muscular layers are apparently unchanged. No ova are found in the small intestine nor in the other tissues. The ova in the walls of the intestine seem much more compressed and distorted than those in the liver. The vessels of the mesentery of the large intestine were carefully searched for the adult parasites, but without success.

Measurements were made of a number of the ova in the tissues, and they were found to average 62 μ in length by 39 μ in width, dimensions which are approximately those give by Stiles, Woolley, Katsurada and

Catto in their accounts of the ova of *Schistosomum japonicum.* They were studied in comparison with a section of the liver from Catto's case, which shows ova of a similar appearance.

III. PATHOGENESIS OF THE CIRRHOSIS OF THE LIVER.

It is clearly evident that in this case the liver was the organ to bear the brunt of the infection, the invasion of the intestinal walls being of but secondary importance to the lesions in the liver. In this respect the findings here are in accord with those hitherto reported in cases of this malady. In the earliest Japanese writings on the disease, the latter is described as a peculiar cirrhosis of the liver due to a parasite, while Katsurada, in his original description, speaks of it as an affection of the liver both of man and of cats. In the case described by Catto, the extreme enlargement of the liver and spleen was noted during life, while at autopsy, although there were marked changes in the other organs, especially in the large intestine, the cirrhotic condition of the liver was perhaps the most striking feature. In Woolley's case, the first to be described in the Philippine Islands, the liver was smaller than normal and markedly cirrhotic. In both of these instances numerous ova were found in the perivascular tissues of the liver, where they apparently caused a marked hypertrophy of the connective tissue. In two of three cases reported by Dr. Logan in China, enlargement of the liver was a prominent feature of the malady while in all three, œdema of the legs and ascites were present, possibly due to hepatic diseases. This list includes all the reported cases that have come to our knowledge, and in practically all of them changes in the liver have been found either clinically or by post-mortem examination.

The pathogenesis of the cirrhosis in these cases is difficult to establish. A moderate increase in the interlobular tissues might be due to the presence alone of the ova, but how can we account for the destruction of whole lobules in the presence of but a very few ova? The anastomosis of the blood vessels within the lobule is so free that it is difficult to see how the ova, acting as emboli, could produce this result, but Katsurada, according to Stiles, believes this to be the explanation of the cirrhosis, although he speaks also of a toxin which he thinks is elaborated by the worm and which plays a part in producing the liver changes.

IV. COMPARISON OF INFECTION WITH SCHISTOSOMUM JAPONICUM AND SCHISTOSOMUM HÆMATOBIUM.

Let us contrast the pathology of the above case with that encountered in Bilharzia infections. Madden, in his excellent monograph on Bilharzia, devotes a score of pages to the pathologic anatomy of the intestinal and urinary tracts, and in four lines disposes of the liver with the statement, "Kartulis and Symmes have described a periportal cirrhosis as having occurred in this disease." Scheube says that the ova have been found in the liver, with slight cirrhotic changes. Manson speaks of the occasional presence of small numbers of ova in the liver, but knows of no pathological change caused by their presence. Other writers on the subject are a unit in regarding the liver as a neglible factor in Bilharziosis.

The question immediately suggests itself, why, in Bilharzia disease, should the ova cause such profound changes in the intestines and bladder, to the practical excluson of alterations in the liver, while, in a disease as closely allied as the one under discussion in our paper, the liver should be the chief site for the lodgement of the ova and its pathology the chief features of the malady?

Dr. Letulle has published an extremely interesting article[3] in which he worked out, with the most faithful attention to details, the histologic changes in a case of intestinal Bilharziosis, and from them drew some convincing conclusions. It is not our purpose to discuss the process of reasoning by which these conclusions were reached, and, therefore, we will give only his explanation of the local distribution of the ova and the resulting pathologic changes. According to his idea the pair of worms, with the female occupying the gynecophoric canal of the male, habitually inhabit the larger venous radicles of the portal system. When the time comes for the deposition of the ova, the worms, still together, migrate to the smaller veins until, having reached such a vessel of a caliber of about 1,000 μ, the male can go no further because of his size. The female then leaves the male and migrates as nearly as possible to the lumen of the intestine or bladder, that is, into the venules of the submucosa where the vessels are narrowed to 80 to 120 μ, and where she can go no farther. She takes position in one of these small veins, completely blocking it, and produces a stasis in the vessels ahead. She attaches herself by her suckers to the intima of the vessel and evacuates her ova into the distal portion of the vein. The pressure of the mass of ova, as well as that of the blood, enable their spines to pierce the walls of the vessels, and the whole mass is forced into the perivascular tissue so quickly, according to Letulle, that although he saw many masses just without the vessel, he did not find a single ovum within the lumen. The female having deposited her ova and waited a sufficient length of time for their migration, joins the male in the large vessels.

Let us apply these facts to *Schistosomum japonicum*. Here we have a similar pair of worms of the same relative size, although both are somewhat smaller than in the Bilharzia species. Although it is not proved that *Schistosomum japonicum* inhabits exclusively or even habitually the arterial side of the pelvic blood supply, Catto found worms in the arterioles in this location, and we have Manson as an authority for their presence on the arterial side. Now let us conjecture that the female, leaving the male in the larger arteriole, migrates into a small vessel which she will just occlude. Attaching herself as in the case of Bilharzia, she deposits her ova, not into a venous radicle, but into the distal side of the arteriole where the ova will be aspirated onward, the more so as in this case they are not provided with spines. Finally they reach the intervening capillaries which have a caliber of perhaps 12 to 20 μ, while the ova which must pass, measure, on the average, 40 μ. If the pressure on the mass of ova is sufficiently great to force a portion of their numbers through the vessel wall, it is not unlikely that another part will be forced through a distended capillary, especially as under the latter circumstances they would be compelled to pass through a distance of no more than 0.5 millimeter before larger venous radicles would be reached, this distance being the average length of a capillary. Having successfully passed the capillaries, nothing would intervene until the liver was reached, where all but the exceptional ovum would lodge. The fact that these exceptions exist, as is proved by the occasional ovum found in the lungs, kidneys and elsewhere, strengthens the evidence of their passing through the capillaries of the pelvis. The marked difference in the pathology of the two diseases, bilharziosis and schistosomiasis, may therefore depend first, on the location of the parasites: the one in the venous and the other in the arterial side of the portal circulation; and, second, on the morphological difference in the ova.[4]

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[3] *Arch. de Parasit.* (1905) **9**, 329.

V. GEOGRAPHICAL LOCATION.

There is nothing in the history of the case we report that is of any assistance toward clearing up the mystery of the mode of infection, nor, on the other hand, anything inconsistent with the theory put forward by the Japanese physicians that the infection is acquired by contact with stagnant water containing the embryos of the parasite. From the relatively small number of ova present it is fair to infer that the infection we studied was of a comparatively recent origin, and that it was acquired after the patient joined the military service. The Scout companies in the Visayas have performed much active duty in the field during the past few years and probably have frequently found it necessary to wade stagnant pools similar to those described by Katsurada as being the habitat of the embryo of this parasite.

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[4] Professor Akira Fujinami has recently published an article on *Schistosomum japonicum* in which he states that the usual habitat of the adult parasite is in the portal system, it having been found by him in the intestinal veins, the mesenteric veins, the branches of the portal vein within the liver, and in the splenic vein. It therefore appears as if the morphology of the ova, rather than the location of the adult parasite, is the chief factor in the distribution of the ova in the tissues of the body.

The most important fact in the history is the continuous residence of the patient in the Visayas and the practical certainty of his having acquired the infection in that part of the Philippine Archipelago.

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ILLUSTRATIONS.

PLATE I.

FIG. 1. Ova of *Schistosomum japonicum* in connective tissue of the liver. ×380.

2. Miliary nodule in the liver. ×100.

3. Nodule showing presence of ova. ×8.

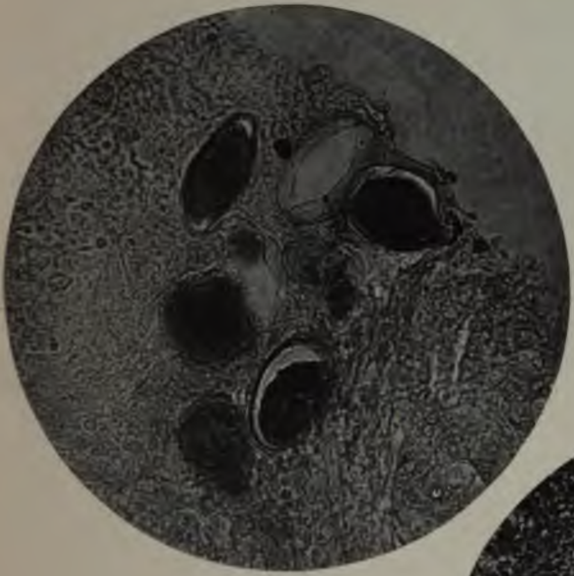

FIG. 1.

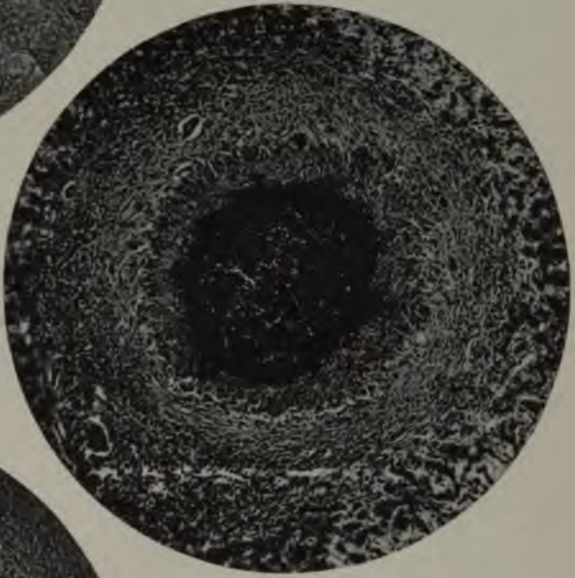

FIG. 2.

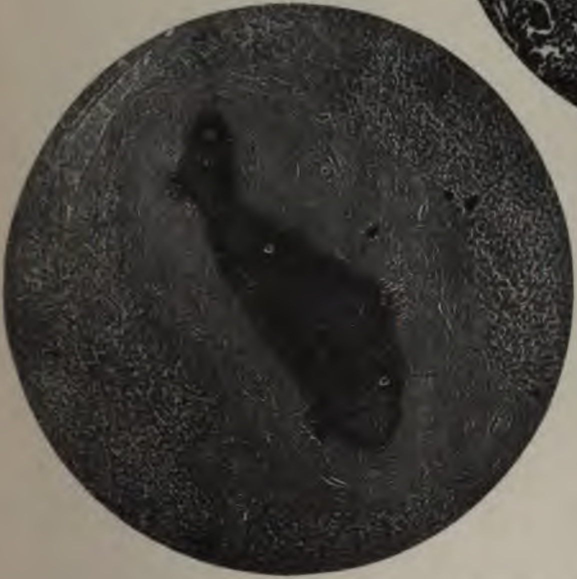

FIG. 3.

PLATE I.

THE DIAGNOSIS OF AFRICAN TICK FEVER FROM THE EXAMINATION OF THE BLOOD.

By RICHARD P. STRONG.

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The study of the various forms of relapsing fever has attracted considerable attention during the past four years. In 1904 P. Ross and Milne, working in Uganda,[1] were able to demonstrate that the disease heretofore known as tick fever and supposedly conveyed by the bite of a tick, was due to a *Spirochæta* which was found in the circulating blood, though usually present here only in very small numbers. Although the disease termed tick fever had been recognized for a long period of time, and was mentioned by Livingstone in 1857,[2] its etiology had previously remained obscure.

In 1905 Dutton and Todd[3] in the Congo were able to confirm the observation of Ross and Milne, and to show that the parasite could pass into the egg and larva of the tick *Ornithodorus moubata* (Murray) and so confer infective power upon the mature form of the succeeding generation. They also frequently found the spirochætæ to be very scanty in the circulating blood. R. Koch,[4] in his studies in Africa in 1905 and 1906 also concluded that the African recurrent fever was transmitted by the bite of the tick *Ornithodorus moubata*. He reported that the malady might be considered an African variety of relapsing fever, but not a distinct and different disease from the European one. He emphasized the fact that the parasites were not numerous in the peripheral blood. He believed that these organisms were usually a little longer than in the case of *Spirochæta recurrens* and that the febrile periods were shorter in the African than in the European variety, but that the two were otherwise similar.

Until the past year (1906) but one distinctive form of relapsing fever in man caused by spirochætæ had been distinguished, although Manson[5] and later Sambon[6] had previously suggested that there might be several forms of this type of disease due to different species of spirochætæ, and Ross and Milne had stated that it was possible there might be more than one variety of tick fever.

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[1] *Brit. Med. Journ.* (1904), 2, 1453.

[2] Mission. Travels and Research: J. Murray, London (1857), 1, 283, etc.

[3] *Brit. Med. Journ.* (1905), 2, Nov. 14, 1259. *Mem. Liv. School Trop. Med.* (1905), 17, 1.

[4] *Deutsche Med. Wchnsch.* (1905), 31, Part II (Nov. 23), 1865. *Berl. klin. Wchnsch.* (1906), 43, 185.

[5] *Brit. Med. Journ.* (1904), 1, 538.

[6] *Brit. Med. Journ.* (1905), 2, 126.

In 1906, Novy and Knapp,[7] after a study of a case of relapsing fever in the United States, concluded that because of morphological characteristics which they were able to detect in stained specimens of the spirochætæ from their own case, and in those of African spirochætæ obtained by them from the Liverpool School of Tropical Medicine, relapsing fever and tick fever are distinct. They also based this claim upon the published experiments of Dutton and Todd and particularly of Breinl and Kinghorn,[8] who found that the spirochæta of the tick variety was frequently fatal to rats and mice and that in rats from three to four relapses occurred before death. Novy and Knapp found that in the case of the spirochæta, which they regarded as *Spirillum obermeieri*, the infection in rats was shorter and that no relapses occurred. They also believed that the diffuse flagella of the organism of tick fever as pictured by Zettnow[9] served as an additional "clinching" proof and effectually differentiated it from *Sp. obermeieri* which had, according to their observations, but a single terminal flagellum. However, according to later observers, Uhlenhuth and Hændel,[10] Novy was not working with *Spirochœta obermeieri*, but with another species, an American variety. Breinl and Kinghorn[11] also found that a monkey and several rats immunized against the American spirochæta (supposed to be identical with *Sp. obermeieri*) remained susceptible to the African species. They were also able to infect a horse, dogs, rabbits, guinea pigs and other animals with the tick-fever parasite. They therefore concluded that the two varieties, American and African relapsing fever, are distinct. Novy and Knapp proposed to differentiate the different species of spirochætæ by serum reactions, specific agglutinins and bacteriolysins, as well as by animal inoculations. Uhlenhuth and Haendel and Frankel,[12] during the present year, and very recently Manteufel,[13] by means of animal inoculations as well as by agglutinative and bacteriolytic reactions, have found that different results are obtained with the European, African and American spirochætæ, and they regard them as three distinct species. Schellack[14] has also very recently recounted the morphological differences in the European, American and African spirochætæ of the recurring fevers.

During a recent visit to the Institut für Schiffs- und Tropenkrankheiten in Hamburg, I had the opportunity, through the kindness of Professor Prowazek, of studying strains of spirochætæ obtained from America and from Africa, and since this time, in different countries, I have examined the other strains of spirochætæ already described in the literature. In the present paper I shall not consider particularly the work in regard to the differentiation of all the spirochætæ of the relapsing fevers, but shall merely record the results of some experiments carried on in relation to the diagnosis and differentiation of the African tick variety of the disease. Ross and Milne,[15] in examining cases of spirillum fever in Uganda, Africa, found that the organism might be exceedingly rare in the blood, even when the examination was made at the height of the fever and from cases which from a clinical standpoint were well marked. Sometimes it was necessary to spend several hours before finding a single spirillum, and in some instances only two or three were found in the whole blood film. In one case of tick fever out of eight which were studied, about one spirillum was found in every thirty fields, in the other seven very few spirilla were present. These authors refer to the fact that Daniels examined a case of the disease in the second week with negative results. Dutton and Todd, R. Koch and Manson all agree that the parasites in tick fever are much more scanty than in European relapsing fever. I observed a patient in Africa who was in approximately the second week of fever, in whom no spirochætæ could be found in the circulating blood in a single, but careful and prolonged examination of the fresh film and of one stained preparation. However, a small amount of blood collected at the same time that the microscopic specimens were examined, was inoculated into a mouse and three days later spirochætæ were found in its blood. Therefore, it is clear that in some cases of tick fever, during its active periods, a diagnosis may not be arrived at from a study of the blood with reference alone to the presence of spirochætæ. Moreover, in both the European and African varieties of the disease, the parasites may be entirely absent from the blood during the relapses or in the later stages, and then even animal inoculations may fail as a means of diagnosis. It is also true in relation to the employment of animal inoculations as a means of diagnosis, white or gray mice, or white rats, the animals which are most valuable for use in this connection, are usually very scanty or impossible to obtain in most tropical or subtropical countries. I have recently been able to show that wild mice captured in these districts are not sufficiently susceptible to infection with the African species of spirochætæ to be of value for use in diagnostic purposes. In addition, neither of these means permits of a differentiation of the species of spirochætæ and of the separation of tick fever from the other forms of relapsing fever. Hence, other methods of diagnosis are desirable.

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[7] *J. Am. Med. Ass.* (1906), **46**, 116. *J. Infect. Dis.* (1906), **3**, 291.

[8] *Lancet* (1906), March 10, 668. *Mem. Liv. School Trop. Med.* **20**, 61.

[9] *Ztschr. f. Hyg. u. Infectionskrankh.* (1906), **52**, 539.

[10] *Arb. a. d. k. Gsndtsamte* (1907), **26**, Heft I, 1.

[11] *Lancet* (1906), June 16, 1690. *Mem. Liv. School Trop. Med.* (1906), **20**, 61, 69, and **21**, 1.

[12] *Berl. klin. Wchnschr.* (1907), **44**, 681.

[13] *Arb. a. d. k. Gsndhtsamte* (1907). **27**, Hefte II, 327.

[14] *Arb. a. d. k. Gsndhtsamte* (1907), **27**, Hefte II, 364.

As long ago as 1896 and 1897 Gabritschewsky[16] and Loventhal[17] suggested and employed the serum for diagnostic purposes in cases of relapsing fever. They recommended that a drop of serum of the patient to be tested and which contained no visible spirochætæ be added to a drop of blood of a patient known to be suffering with relapsing fever and in whose circulation the parasite was present. The bactericidal action of the first serum was then observed under the microscope for various periods of time. Later Karlinski,[18] Routkewitsch,[19] Mielkich [20] and particularly Hodlmoser [21] also employed this method for diagnostic purposes in European relapsing fever, although not always with favorable results. Hodlmoser emphasized the fact that in the sero-diagnostic method of European relapsing fever, the most striking feature is the spirolytic action of the serum rather than the agglutinative one. While he believed that the reaction could not be obtained with absolute certainty in all cases of relapsing fever, it nevertheless constituted in many a valuable means of diagnosis. In all of these experiments the blood of another patient containing spirochætæ was employed in making the test of the suspected patient's serum. Hence, fresh cases of relapsing fever in human beings were always necessary in order that the test might be performed. It therefore naturally occurred to me that an examination of the blood serum in African tick-fever infections for specific agglutinins and bacteriolysins might sometimes prove of additional value in obtaining a diagnosis, the blood of animals infected with the spirochætæ instead of that of human beings being employed in testing the serum. However, I found that while sometimes by means of the agglutination or bacteriolytic reaction a satisfactory result might be obtained with an immune spirochætæ serum, nevertheless it soon became apparent that the reaction was frequently too uncertain and inconstant to be depended upon for diagnostic purposes. Moreover, it could not be considered to be of any practical use to the average physician.

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[15] *Loc. cit.*

[16] *Ann. Inst. Past.* (1896), **10**, 630.

[17] *Deutsche med. Wchnsch.* (1897), **23**, 560.

There are many difficulties to be encountered in performing the agglutinative and spirolytic test with the spirochætæ of this group, and it is perhaps unnecessary to emphasize that the reaction can not be carried out with nearly the same facility as the agglutination reaction with immune sera and bacteria. Perhaps the greatest difficulty is experienced in securing the proper culture of the spirochætæ in the blood to be used in testing the agglutinative and bacteriolytic power of the serum of the affected patient. While, in general, it may be stated that the white mouse is the most suitable animal to employ and that the blood containing spirochætæ should be collected in citrate solution on the second or third day after infection, because the parasites are apt to be most numerous and most active at this period of time, nevertheless it frequently occurs that the blood of the animal when taken at these periods contains too few spirochætæ to render the test satisfactory or conclusive, and this may occur although the animal was previously inoculated with a large amount of blood richly infected with spirochætæ. In some instances the spirochætæ in the blood may appear to be ideal for the performance of the test, the parasites being numerous, active and not agglutinated, yet when they are added to a normal serum they may undergo spontaneous agglutination as marked as if an immune serum had been employed. Again, in some instances in the same period of time that they become agglutinated and clumped in the immune serum, they may undergo the same apparent process in their own serum, without the addition of that of the blood to be tested. The parasites at other times may appear to be very numerous in the blood at the time of the examination and in the few minutes required to bleed the animal they may apparently all disappear before anything is added to the blood. These phenomena may be understood at least partially when one considers that in the infected animal the agglutinins and spirolysins are being developed gradually with the development and increase in number of the spirochætæ, and hence in animals which show a very rich infection with spirochætæ, agglutinins and spirolysins are already present to a greater or less extent. Sometimes the withdrawal of the blood seems to be all that is necessary to stimulate the complements and antibodies to action and in other instances the additional amount of these corresponding substances, either present in the normal or immune serum, may be necessary to bring about the phenomenon of agglutination or of bacteriolysis. Sometimes it will be necessary to take the blood from several animals before one is found in which a satisfactory condition of the spirochætæ exists for the performance of the agglutinative or bacteriolytic test. Indeed, on some occasions it has taken me three or four days before satisfactory conditions for even the proper performance of these tests could be obtained. Obviously, the employment of the spirolytic test in the abdominal cavity of an animal presented even greater difficulties. It therefore seemed highly desirable that some other means be found that would serve as an aid in the diagnosis of the disease and in the differentiation of its different varieties, and I determined to see if the precipitin reaction might be employed for this purpose. Evidently if this reaction could be shown to be satisfactory for this purpose the diagnosis of this group of diseases would be much simplified and at once placed upon a practical basis.

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[18] *Wien. klin. Wchnsch.* (1903), **16**, 447. *Centrbl. f. Bakteriol.* (1902), **1**, 31, 566.

[19] *Baumg. Jahresb.* (1898), **14**, 613. Original article in ***Russiches archives d.*** *Pathol.* etc. (1898), July 5.

[20] *Baumg. Jahresb.* (1900), **16**, 434.

[21] *Wien. med. Wchnsch.* (1904), **54**, 2310. *Ztschr. f. Heilk. Abt. Interne Med.* (1905), new series 6, 506.

As is well known, Kraus[22] in 1907 first showed the existence of specific precipitins for the albuminous bodies found in bacterial cultures. Later it was demonstrated that the reaction might be employed for the differentiation from one another of the vibrios of Finkler and Prior, Nasik, Denecke, and of Metchnikoff, and also for differentiating colon from paracolon bacilli. Wladimiroff[23]

[22] *Wien. klin. Wchnsch.* (1897), **10**, 736.

[23] Kolle und Wassermann Handbuch d. pathogen Mikrorgan. (1904), **4**, 1055.

employed the reaction in the diagnosis of glanders, using a glycerine-free culture filtrate of *Bacillus mallei* added to the serum of the glandered horse. The employment of the reaction with sera prepared by injecting into one animal certain albuminous bodies of another one has also proved of great value for diagnostic purposes, and in some instances a very delicate test. Thus Wassermann and Uhlenbuth,[24] with proper immune sera, showed that a specific precipitin reaction might be obtained against the dissolved albuminous substances in human blood in the dilution of 1 to 50,000. The precipitins have been proved to be absolutely specific against those of unrelated species, although they sometimes react on closely related albumens. The reaction has also been employed for the differentiation of other microörganisms, including bovine and human strains of tubercule bacilli and even for the various species of trypanosomata, with varying results. Shortly after my experiments were begun with the precipitin test in the diagnosis of the spirochætæ of relapsing fever, the work of Fornet, Shereschewsky, Eisenzimmer and Rosenfeld,[25] on the subject of "Spezifische Niederschläge bei Lues Tabes und Paralyse" appeared. These authors found that upon mixing the serum from acute cases of syphilis with that from cases of the same disease of long standing, with tabetic and paralytic symptoms, that a precipitin was obtained. They believed that in the more acute cases of syphilis, those in which spirochætæ were found to be present, the precipitinogen was present in the serum and that in the older cases of long standing the precipitin existed. They employed the ring test for these reactions, placing the heavier serum at the bottom of a small test tube and adding gradually the lighter serum in a layer on top. At the junction of the two sera in the case of a positive reaction, the precipitate appeared as a narrow band or ring. Still more recently Michaelis[26] has reported that he obtained a specific precipitin reaction with the blood sera in cases of syphilis, employing an extract of the liver as the solution containing the precipitinogen.

The experiments to be recorded here were conducted with two strains of spirochætæ, one obtained from Africa and the other from America. At first the precipitin reactions were carried on in small, conical reagent glasses by mixing the serum supposed to contain an excess of precipitinogen with the immune serum supposed to contain an excess of precipitin. The resulting mixture was then compared with one consisting of the first serum to which a normal serum had been added. After reading the article of Fornet and his colleagues, the reactions were carried on by superimposing one serum upon the other, as was suggested by these authors, the second serum being allowed to flow down the side of the reagent glass from a capillary pipette until a layer of equal thickness to that of the first below had been introduced. Care was taken to observe that the blood from which the serum was separated and used for the precipitin contained no spirochætæ which could be detected by microscopical examination, both before and at the time the blood was collected for the test, and that the blood from which the serum was separated for use as the precipitinogen contained numerous parasites.

[24] *Loc. cit.*, 594.

[25] *Deutsche med. Wchnsch.* (1907), **33**, 1679.

[26] *Berl. klin. Wchnsch.* (1907), **44**, 1477.

The blood serum tested for the precipitin was collected from animals which had received one, two and three separate infections of spirochætæ respectively, and from which the spirochætæ had disappeared so far as could be determined by microscopical examination.

Since it has been observed in the study of the precipitin reaction that the precipitin is sometimes soluble in an excess of precipitable substance, and that there must exist a certain quantitative relationship between the amount of precipitin and precipitable substances for the optimum reaction, many of these experiments were also performed in various dilutions of the sera. Finally, these same sera were examined for the presence of agglutinins, and in some instances for bacteriolysins.

The following series of experiments illustrates the value of the precipitin reaction for diagnostic purposes in this disease.

EXPERIMENTS.

SERIES NO. 1.

Mouse No. 1 inoculated on two different occasions with African *Spirochæta recurrens;* the last inoculation ten days previously. Microscopic examination shows no spirochætæ in the circulating blood.

Mouse No. 2 inoculated on two previous occasions with the American spirochæta; the last inoculation twelve days previously. Microscopic examination of blood negative for spirochætæ.

Mouse No. 3 inoculated three days previously with the African spirochæta. Microscopic examination shows very few spirochætæ present in the circulating blood.

Mouse No. 4 inoculated three days previously with the American spirochæta. Microscopic examination shows very rich infection with spirochætæ.

All four animals were bled to death; the blood placed on ice over night;[37] the next morning it was centrifugated, the serum drawn off from the clot and recentrifugated in each instance. All sera were obtained clear. The following reactions were performed:

Conditions of reaction.		Precipitin reaction.
Serum of—	Plus serum of—	
Mouse 1 (immune to African S.)	Mouse 3 (infected with African spirochæta)	Negative.
Mouse 1 (immune to African S.)	Mouse 4 (infected with American spirochæta)	Slight clouding of the mixture of sera.
Mouse 2 (immune to American S.)	do	Negative.
Mouse 2 (immune to American S.)	Mouse 3 (infected with African spirochæta)	Do.
Normal mouse	do	Do.
Normal mouse	Mouse 4 (infected with American spirochæta)	Do.

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[37] It was thought advisable to allow the blood containing the spirochætæ to stand over night in order to aid in the breaking up of the spirochætæ and thus favor the passing of the soluble albumens into the serum.

Remarks.—Only in one instance is there a suggestion of a reaction, and this is between the American spirochæta and the African immune serum. With the African spirochæta and the African immune serum there is no evidence of a reaction. However, since the parasites were very scanty in the serum containing African spirochætæ, it is possible there was not sufficient precipitinogen present to give rise to a precipitate.

SERIES NO. II.

Experiments with the African strain.—Rats numbered 1, 2 and 3 having had one inoculation of African spirochætæ twelve days previously, were inoculated November 8 each with 0.25 cubic centimeter of mouse's blood, containing fairly numerous African spirochætæ, diluted with saline solution. November 11, microscopical examination; no parasites were found in the blood of any of the rats. Evidently relatively immune to the infection.

Rats numbered 4, 5, 6 and 7 (all normal rats) were each infected on November 8 with 0.25 cubic centimeter of the same mouse's blood containing African spirochætæ used to immunize rats numbered 1, 2 and 3. November 11 one rat, number 5, has succumbed. In numbers 4 and 6 a few spirochætæ are present in the blood. In number 7 the parasites can not be found.

November 12 a blood examination of rats numbered 1 and 2 again shows no spirochætæ to be present. The animals were bled to death, the blood put aside for one and one-half hours and then centrifugated and the serum drawn off. A blood examination of rats numbered 4, 6 and 7 shows in each instance fair numbers of spirochætæ; more were found to be present than in the examination of November 11. Numbers 4 and 6 were also bled to death, the blood centrifugated, placed aside for a few hours and the serum drawn off.

Experiments with the American strain.—Mice numbered 8 to 14 have had one previous infection with American spirochætæ ten days previously; they were reinoculated November 8, each with 0.125 cubic centimeter of mouse's blood, containing numerous American spirochætæ, diluted with saline solution. November 11 an examination of the blood shows the absence of spirochætæ in the circulating blood. The animals are evidently immune.

November 8, rats numbered 15 to 18, normal rats, each infected with 0.25 cubic centimeter of mouse's blood containing numerous American spirochætæ. This same blood was used to immunize mice numbered 8 to 14.

November 11 all of these rats (numbered 15 to 18) are found to be infected with spirochætæ, although only a few of the parasites are present in the circulating blood.

November 12 an examination of mice numbered 8 to 14 shows no spirochætæ in the circulating blood. Numbers 8 to 12 were bled to death and serum collected. Rats numbered 15 to 18 were also examined, only one, number 15, shows a rather rich infection, while the others show very few parasites, although more are present than on November 11. Rat number 15 was bled to death and the serum collected.

The following precipitin reactions were performed with the sera of the above animals:

Conditions of reaction.		Precipitin reaction.
Serum of—	Plus serum of—	
Rat 1 (immune to African *S*)	Rat 4 (infected with African *S*)	Negative.
Rat 2 (immune to African *S*)	Rat 6 (infected with African *S*)	Do.
Rat 1 (immune to African *S*)	Rat 15 (infected with American *S*)	Do.
Rat 2 (immune to African *S*)	do	Do.
Mice 8 to 10 (immune to American *S*)	do	Do.
Mice 11 and 12 (immune to American *S*)	do	Do.
Mice 8 to 10 (immune to American *S*)	Rat 4 (infected with African *S*)	Do.
Mice 11 and 12 (immune to American *S*)	Rat 6 (infected with African *S*)	Do.

Remarks.—There was no trace of a reaction in any of the tubes after two hours, after eighteen hours, or even after forty-eight hours.

November 13 another of the rats, number 17, infected with American spirochæta on November 8, shows numerous spirochætæ in the circulating blood. The animal was bled to death. Some drops of the fresh blood were mixed with citrate solution; after fifteen minutes the parasites had disappeared and could no longer be found on microscopic examination. It seems probable that the blood was collected just before the crisis, that the parasites were about to undergo bacteriolysis, and that the withdrawal of the blood hastened this reaction. The remainder of the blood collected was centrifugated and the serum separated.

The following precipitin reactions were performed, the serum of rat number 17 being used for the precipitinogen.

Conditions of reaction.		Precipitin reaction.
Serum of—	Plus serum of—	
Rat 1 (immune to African *S*)	Rat 17 (infected with American *S*)	Negative.
Rat 2 (immune to African *S*)	do	Do.
Mice 8 to 10 (immune to American *S*)	do	Do.
Mice 11 and 12 (immune to American *S*)	do	Do.

Remark.—No trace of a reaction occurred in any of the tubes after two and after twenty-four hours.

In order to be sure that antibodies were already present in the sera of animals numbered 1 and 2 and 8 to 12, attempts were made to test the agglutinative value of the sera with the blood of mice numbered 19 and 20, which had been infected two days previously with African spirochætæ and with the blood of rat number 17, the blood of which showed a rich infection with American spirochætæ. However, although the reactions were performed with the blood of mice numbered 19 and 20, there were too few parasites present to allow me to arrive at any definite conclusions, and as has already been stated, the parasites disappeared from the blood of rat number 17 a few minutes after its withdrawal. As the examination of the blood of all the other infected animals on hand on this date showed none containing parasites in a satisfactory condition for the performance of the agglutination or bacteriolytic test, these reactions could not be performed satisfactorily.

SERIES NO. III.

Experiments with the African spirochæta.—Mice numbered 1 and 2 had been infected about one month before with the African spirochæta. A blood examination on November 8 showed no parasites to be present. The animals were bled to death and the serum separated.

Mice numbered 3 and 4 were infected with the African spirochæta on November 5. A blood examination on November 8 showed the parasites to be very numerous. The animals were bled and a small quantity of the blood mixed with citrate solution for agglutination reactions. The serum was separated from the remainder.

Experiments with the American spirochæta.—Mice numbered 5, 6 and 7 had been infected about one month before with the American spirochæta. A blood examination on November 8 showed no parasites. .The animals were bled to death and the serum separated.

Mice numbered 8 and 9 were infected with American spirochætæ on November 5. A blood examination on November 8 showed a fair number of parasites present. The animals were bled to death and a small quantity of the blood mixed with citrate solution for agglutinative reactions. The serum was separated from the remainder.

The following agglutination reactions were performed:

Conditions of reaction.		Agglutination.	
Serum of—	Plus citrated blood of—	1-5.	1-10.
Mice 1 and 2 (immune to African *S*).	Mice 3 and 4 (infected with African *S*).	Marked after 15 minutes.	Marked after 15 minutes.
Mice 1 and 2 (immune to African *S*).	Mice 8 and 9 (infected with American *S*).	No agglutination but too few parasites present for a decisive test.	
Mice 5, 6, 7 (immune to American *S*).	Mice 3 and 4 (infected with African *S*).	Negative after 15 minutes; after one-half hour moderate agglutination.	Practically no agglutination.
Mice 5, 6, 7 (immune to American *S*).	Mice 8 and 9 (infected with American *S*).	Parasites too scanty to judge definitely of reaction, few found scattered. Not agglutinated.	

The following precipitin reactions were performed with the same sera:

Conditions of reaction.		Precipitin reaction after 8 hours.
Sera of—	Plus sera of—	
Mice 1 and 2 (immune to African *S*)	Mice 3 and 4 (infected with African *S*)	Negative.
Mice 1 and 2 (immune to African *S*)	Mice 8 and 9 (infected with American *S*)	Do.
Mice 5, 6, 7 (immune to American *S*)	do	Do.
Mice 5, 6, 7 (immune to American *S*)	Mice 3 and 4 (infected with African *S*)	Do.

Remarks.—The precipitin experiments performed in duplicate and in dilutions of the different sera of 1 to 5 and 1 to 10 were all negative. However, it is to be noted that agglutinins had already developed in some of the sera.

On November 11 the following further agglutinative reactions were performed with the same sera of animals numbered 1 and 2, and 5, 6 and 7; the citrated blood of mice numbered 10 and 11, infected with spirochætæ on November 8, being used to furnish the spirochætæ which were numerous and very active at the time of the test:

Number.	Conditions of reaction.		Agglutination.
	Sera of—	Plus citrated blood of—	
I	Mice 1 and 2 (immune to African *S*).	Mouse 10 (infected with African *S*).	Positive good clumps and star forms in 5 to 10 minutes in dilutions of 1-10 and 1-20. Parasites have lost almost entirely their motility.
II	Mice 5, 6, 7 (immune to American *S*).	do	Negative. Parasites retain their motility and remain singly. No clumps or agglutination in dilutions of 1-5, 1-10.
III	Mice 5, 6, 7 (immune to American *S*).	Mouse 11 (infected with American *S*).	Positive. Very large clumps and balls of organisms in 5 minutes. Marked reactions in dilutions of 1-10 and 1-20.
IV	Mice 1 and 2 (immune to African *S*).	do	Negative. Organisms remain single even in dilutions 1-2 and 1-10; also still motile.

Remarks.—The above reactions were observed in moist preparations and were confirmed also by stained ones. In experiments I and III, in the dilution 1 to 2, the agglutination was not so visibly marked because of the spirolytic action of the sera on the spirochætæ.

SERIES NO. IV.

Experiments with the African spirochæta.—November 15, rat number 1 which had received two previous injections with African spirochætæ on October 4 and November 8 was again inoculated November 15 with blood containing numerous African spirochætæ.

Rat number 2, which had been given one previous injection of the African spirochæta on November 8, was again inoculated November 15 in the same manner as rat number 1.

Rat number 3, which had not been previously injected with spirochætæ, was also inoculated on November 15 in the same manner as rats numbered 1 and 2.

Experiments with the American spirochæta.—Rat number 4, which had received two previous injections with American spirochætæ on October 4 and November 8, was again inoculated on November 15 with blood containing numerous American spirochætæ.

Rat number 5, which had been given one previous injection with the American spirochæta on November 8, was again inoculated on November 15 in the same manner as rat number 4.

Rat number 6, which had not previously been inoculated with spirochætæ, was also injected on November 15 in the same manner as rat number 4.

On November 17 a blood examination of all the animals was made. In rats numbered 1 and 4 no parasites whatever were found; in rats numbered 2 and 3 very few parasites were seen; in rats numbered 5 and 6 a moderate number of parasites were encountered. On November 18 no parasites were found in rat number 2 but in rat number 3 they had increased in number; in rat number 5 they were still present.

November 21, rat number 7, a normal rat, was injected with African spirochætæ and rat number 8, a normal rat, with American spirochætæ. On November 23 microscopical examination showed rats numbered 1 to 6 all to be free from parasites; rats numbered 7 and 8 each showed moderate infections with spirochætæ. The animals were all bled to death and the serum separated.

The following precipitin reactions were performed:

Conditions of reaction.		Precipitin reaction.
Serum of—	Plus serum of—	
Rat 1 (immune to African *S*)	Rat 7 (infected with African *S*)	Negative.
Rat 2 (immune to African *S*)	Rat 7 (infected with African *S*)	Do.
Rat 3 (immune to African *S*)	Rat 7 (infected with African *S*)	Do.
Rat 4 (immune to American *S*)	Rat 8 (infected with American *S*)	Do.
Rat 5 (immune to American *S*)	Rat 8 (infected with American *S*)	Do.
Rat 6 (immune to American *S*)	Rat 8 (infected with American *S*)	Do.
Rat 1 (immune to African *S*)	Rat 7 (infected with African *S*)	Do.

The following agglutination reactions were performed:

Conditions of reaction.		Agglutination, dilutions 1 to 10
Serum of—	Plus citrated blood of—	
Rat 1 (immune to African *S*)	Rat 7 (infected with African *S*)	Strong reaction.
Rat 1 (immune to African *S*)	Rat 8 (infected with American *S*)	Negative.
Rat 2 (immune to African *S*)	Rat 7 (infected with African *S*)	Strong reaction.
Rat 5 (immune to American *S*)	Rat 7 (infected with African *S*)	Negative.
Rat 5 (immune to American *S*)	Rat 8 (infected with American *S*)	Positive reaction.
Rat 6 (immune to American *S*)	Rat 8 (infected with American *S*)	Negative.

The above-described experiments demonstrate that the precipitin reaction in the manner employed is of no value for the purpose either of the differentiation of the spirochætæ of relapsing fever or for the diagnosis of the infection. It would appear from the series of experiments numbered 3 and 4, that during immunization with these spirochætæ, as in some bacterial infections, the agglutinins and bacteriolysins become developed in demonstrable quantities more quickly than the precipitins. It is very probable that an animal might be sufficiently highly immunized so that a precipitin test for these spirochætæ could eventually be obtained; but the above experiments conclusively demonstrate that this test is not a practical one as a means of diagnosis of the infection.

It may be stated in relation to the employment of the agglutinative test for this purpose, that, as has already been pointed out, owing to the difficulties of technique in performing the reaction and to the fact that in tick fever infections the agglutinins sometimes do not become developed until after several relapses or reinfections with the spriochætæ have occurred (a fact to which Manteufel [28] recently called attention for infections with *Spirochæta obermeieri*) the agglutinative reaction even in low dilutions also does not constitute a satisfactory means of diagnosis.[29]

For the present, the most efficacious methods at our disposal are the microscopic examination of the peripheral blood and of that obtained by puncture of the liver and spleen, both in fresh and in stained preparations, and by animal inoculations with the blood when suitable species are at hand for this purpose. Usually, a marked polymorphonuclear leucocytosis occurs, frequently before the crisis, and it usually persists for a day or two after it. At the latter time, an increase of the large mononuclear cells may be encountered. It should be remembered that even in cases well marked from a clinical standpoint, the microscopic specimens of the centrifugated blood may be examined an hour or two before a single parasite is finally discovered. If the parasites are not found by the examination of the blood, inoculations of white mice, white rats or monkeys with the blood of the suspected patient should be carried out if practicable. If the spirochætæ develop in the blood of the animal, they may if it is thought desirable be differentiated by means of specific agglutinating sera. Clinically, it is sometimes quite impossible to distinguish African tick fever from several other febrile infections.

I have seen in a hospital at one time as many as five cases diagnosed as spirochætal fever infections by a competent physician, thoroughly familiar with the clinical picture of relapsing fever and accustomed to seeing numerous cases of this disease. I was unable to find a single spirochæta in the blood of any of these patients.

Theoretically, it is very easy to distinguish tick fever from typhus fever, malaria, trypanosomiasis and *Kala-azar* by the blood changes. In practice, this is at times most difficult, and the individual case may require considerable study before a correct diagnosis can be made.

In conclusion, I wish to express my thanks to Professor Nocht, Professor Fullerborne, Professor Geimsa and Professor Prowazek, for many courtesies extended to me during my stay at the Institut für Schiffs- und Tropen-Krankheiten, where most of the laboratory experiments described in this paper were performed.

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[28] *Loc. cit.*

[29] No attempt was made to employ the reaction of the deflection of the complement for diagnostic purposes in these spirochætæ infections, for the reason that it appears that the definite value of this reaction has not as yet been entirely determined for bacterial infections.

OBSTETRICS IN THE PHILIPPINE ISLANDS.

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INTRODUCTION.

More than two years ago, in a lecture which I gave in the *Liceo de Manila*, by request of the *Asociación Feminista Filipina*, I had an opportunity to express my personal opinions on the interesting problem of infant mortality in Manila and at the same time to propose means for ameliorating this condition. I believed the most efficacious measure, along with popular education, to be the organization of a good service of midwives, with a lying-in dispensary to which the poor women of this city could go for assistance. In this manner we would remedy the necessity which compels women, neglected by fortune, to give birth to their children in miserable habitations lacking every hygienic facility and to place their lives and those of their new-born infants at the mercy of ignorant midwives, audacious in the abuse of obstetrical practice. It is necessary to establish a school for midwives who, when sufficiently instructed, would be excellent disseminators of the teachings derived from the practice of modern obstetrics.

The suggestion then made did not fall on barren soil, for the Philippine Commission, at the instigation of Dean C. Worcester, Secretary of the Interior, appropriated the funds necessary for the building in Manila, within a short time, of a pavilion hospital planned according to modern standards. One of these pavilions will constitute the beginning of the future lying-in hospital of Manila.

However, we are confronted by another question of equal importance. When the obstetrical pavilion is erected, can we count on the women of the lower classes, who form the majority of the population of these Islands, attending this new clinic and renouncing once for all the irrational practices of ignorant midwives and illegal practitioners? Before we can respond in the affirmative, it will be necessary for the Philippine Medical School and the Bureau of Health to agree to lead and direct the education of these ignorant women into new channels, overthrowing routine customs and traditional means, many of which I shall briefly discuss in this analytical study of obstetrics in the Philippines.

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[1] **Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, Manila, February 29, 1908.**

EARLY SUPERSTITIONS.

During many centuries the mission of assisting in childbirth was confined exclusively to midwives, who were the oldest women of the community in which they resided and who, taught by their own personal experience, advised and aided the young and inexpert. A certain number of precepts acquired by experience and observation, and a still larger number of individual practices and superstitions, represented the whole fund of knowledge employed in difficult cases. These midwives, who in primitive times existed in all countries, are still known in the Philippines by the name of *hilot,* a Tagalog word which has come down to us through many generations, in the same manner as the term *salag*, by which is known the person who assists the *hilot* in her empirical manipulations.

The conjunction of the moon, the appearance of comets, the flow and ebb of the tides, the direction of the winds and the influence of heat and cold were, for the *hilot* and *salags*, the etiologic agents which decided the development of pregnancy, or the evolution and progress of childbirth.

In view of such prejudices, it is not surprising that even in the most aggravated cases of dystocia, the unfortunate patient was abandoned to the sole efforts of nature, any rational intervention for saving her from certain death being absolutely unknown. Failure was attributed by the midwife to the fatal influence of the *asuang*, a malignant spirit which, according to the common people, lies in wait for pregnant women and, at the moment of labor, penetrates into the uterus to devour the fœtus; just as another spirit called *patianac,* in the shape of a strange animal, introduces itself into the genitals of pregnant women in order to devour the product of conception. The influence of the *patianac* was to the midwife the logical explanation of the pathologic phenomena of pregnancy, which we now know as abortion, expulsion of a macerated fœtus, uterine mole, *placenta prœvia*, etc. In my opinion, these superstitions have their origin in the ancient beliefs of paganism predominating in the Philippine Islands before the arrival of the Spaniards, and they gained such a hold on the minds of the people that they are still preserved latent in some parts of the Archipelago, and have on some occasions given rise to barbarous practices and manipulations which are an outrage to civilization and which have cost the lives of many women in childbirth.

While I was an interne in the San Juan de Dios Hospital in the year 1889, I performed an autopsy on a poor woman who had died in the district of Tondo because a quack had barbarously beaten her with the tail of a sting-ray. This woman, after a normal delivery, had contracted puerpal fever, and the violent chills which seized her were attributed by the quack to the presence of the *asuang*, which needed to be driven out of her by a severe whipping with some bruising instrument which, like the tail of the sting-ray, had the medicinal virtue of expelling all malignant spirits.

INFLUENCE OF THE MISSIONARIES.

At a later period, bearers of a new civilization arrived on these shores in the shape of the Spanish missionaries or friars. These representatives of the church spread throughout the villages of the Philippines and there they organized parishes. These holy men, ministers of a religion which is all peace and charity, could not long remain indifferent to the ailments of the body, and in the same manner as that in which they ministered to the afflictions of the soul, the woman in the throes of childbirth was also made the object of their solicitous care.

In order to give a slight idea of remedies which were used by the friars in these early days, I will here transcribe a curious chapter from the work of Father Pablo Clain, S. J., entitled "Easy Remedies for Various Diseases." The work was published in Manila in the year 1710, being practically two centuries old. The chapter mentioned, which is entitled "Parturition, How to Facilitate it," reads, literally translated, as follows:

> "Cause the woman about to give birth to sneeze, by blowing into her nostrils some of the powder known as *Verbo apoplegia*, or mustard seed, and white pepper. Give her a spoonful of mass wine from time to time, or give her to drink, in tepid water, the balls of hair formed on deer or hogs (weight of nine or ten grains of pepper).
>
> "As to the exterior, the midwife should frequently anoint the abdomen with tepid coconut oil, mixed with *escobilla juice*[2] (*Sida carpinifolia* L.).
>
> "Apply to the abdomen fomentations of a decoction of emollient herbs, such as *escobilla, mallows, castiogan* root (*Hibiscus abelmoschus* L.), *camantigue* leaves (*Impatiens balsamina* L.) and costmary (*Tanacetum balsamita* L.). Give her acrid and irritating injections. Some praise the gall of a black hen applied to the navel; others mouse excrements dissolved in tepid wine or tepid water given to drink (as high as six grains). *A duferro*[3] stone should be tied to the thighs (or applied to the lower parts); but it should be removed immediately after the placenta has been expelled. A loadstone tied to the thigh, on the inner side, is likewise efficacious. If the new-born infant is weak, strengthen it by giving the mother a swallow or spoonful of tepid Castile wine, and externally, by placing on her abdomen a piece of toasted bread, sprinkled with hot mass wine and powdered cloves, cinnamon and nutmeg. If the child begins to emerge in an unfavorable manner, such as presenting first an arm or a foot,

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[2] The scientific names of the plants mentioned have been supplied by Dr. Leon Guerrero and by Mr. Merrill, Bureau of Science.

[3] A translation of this word can not be supplied.

or in some other manner, the midwife must push it back inside of the mother, who must then lie on her back, with the head low and the nates raised, and after having put back the arm or foot which the child presented, the midwife must make it retrocede by gently pressing the abdomen of the pregnant woman upwards and towards the epigastric region, or the breast, and after the child is again within, she must manipulate it so that it will emerge in due form; the midwife endeavoring, using her hands, to make the child turn its face towards the back of its mother, and then by raising its nates and legs to the navel of the mother, to have it emerge in the proper manner.

"The common people use the following remedies: They make the parturient drink some of the milk of a woman nursing a child, or make her suck the nipples of such a woman; they cautiously apply to her body a snake skin shed by a snake, but remove it as soon as she has been delivered, because otherwise her entrails might come out. On the groins they put bruised *salibutbut* (*Tabernæmontana Pandacaqui* Poir.), warming it in hot ashes. The parturient is made to drink costmary juice in strong wine. She is given mint, bruised and mixed with water and honey, and forced to drink a decoction of *raiz oriental* (*Andropagon nardus* L.), *palasan* (*Calamus albus* Pers.) and panara plantain in water, as well as to drink bezoar taken from a deer or wild hog, burned on a potsherd and dissolved in a little wine or water. If the patient has any strength left, she is made to drink dog urine, or horse or cow excrements, three *reales* weight, dried, crushed and mixed with water or wine; this is also useful for ejecting a dead infant. She must hold a jasper stone in her hand. She is given sweet-basil juice (*Ocimum basilicum* Linn.) to drink."

However ridiculous these prescriptions may seem, the fact remains that they were faithfully observed and carried out in the treatment of many parturients, for the reason that they had come from the authoritative lips of a missionary priest, compelled by the force of circumstances to serve as physician as well. It was for good reasons that the Reverend Father Gregorio Sanz, of the Barefooted Order of Saint Agustine, writes as follows in his treatise on "Sacred Embryology" (p. 39), edited in Manila in the year 1856:

"In the Philippine Islands, where in a way it may be said that outside of the capitals there is no physician but Providence, nothing was more common than to see the curates practice medicine among the natives of their parishes, whether the latter were men or women."

On pages 167 and 168 he adds the following words:

"The number of midwives in a parish having been ascertained, it is advisable to communicate to them individually the instructions which we give hereinafter, if they have not already received them; it is of the greatest importance to have them well instructed in this respect and for this purpose it is very advisable, in view of the facility with which these good people forget what has been taught them, especially if it be something that they have to practice only a few times, that every year after their first instruction, at the time of the examination in the catechism for the perfection of the parish, they be reëxamined in everything that was taught them upon their admission into the profession of midwifery. If, though this is hardly to be expected, the midwives should object and refuse to receive instruction from their curates on this subject, it will become necessary to notify the civil authorities, in order that they may be [illegible] from their [illegible] and to [illegible] the [illegible] [illegible] in the following manner.”

These words show that in [illegible] times the missionary priests possessed a certain influence over a great number of natives, who took even medical instructions from them. These instructions, it is true, are mainly concerned in everything relating to proper baptism which, in cases of necessity, was administered to the child either within or without the mother's womb; but they also extended to medical aid, the manner of attending parturients. A proof of this is found in the following paragraph taken from the above-mentioned work of Father [illegible] Sanz, relating to the treatment of abortions:

“The first and most important thing is to advise the patient to remain in a recumbent position and to preserve absolute repose of body and mind. The second is to bleed the arm, if the woman is robust, and if she is weak or nervous to apply ten or twelve leeches or cupping-glasses to the breasts, these being the regions best indicated at this epoch. The blood-letting and likewise the application of leeches should be employed only when recommended by a medical person. At the same time a lemonade of cream of tartar, with sugar and small quantity of saltpeter, should be administered and the loins and abdomen should be gently rubbed with hot essence of mastic.

“If the woman is in convulsions, or if she is nervous and suffers very intense pain, then she must be given an antispasmodic potion composed of one ounce of almond oil, another of simple syrup, and one grain of extract of henbane, of which one spoonful must be taken every half hour; at the same time the abdomen should be rubbed with a mixture of one ounce of henbane and one drachm of tincture of opium. Experience has demonstrated that in the majority of cases simple means are sufficient to check abortion at the outset, but as they are not all within the reach of the native midwives, and it is not easy for all to secure them, we shall indicate another remedy which is simpler, but assuredly not so efficacious.

“As soon as the pregnant woman feels the symptoms which we have indicated above she must remain very quiet, speak very little and keep to her bed for several days. Cupping-glasses may be applied to her arms and she may be given copious drafts of common water prepared in this manner: Two ounces of unhusked rice are boiled in half a ganta (1.5 liters) of water until the grains burst open, then the water is strained and two spoonfuls of lemon juice are added.

“She must abstain from eating meat, chicken, eggs and fish; her food should consist of rice broth or *puspas* (stewed rice and meat), of little substance if the patient is robust or sanguine. She may also be given a light enema of a decoction of mallow, with the yolk of an egg; but this is only in cases where the evacuations are accompanied by tenesmus, or where the bowels have not moved for many days.”

The same author, who is more modern than Father Clain and who seems to be inclined toward surgery, in an address to his colleagues, the parish priests, wrote the following in connection with the Cæsarian section performed after the death of the mother:

“Every curate should secure the proper instrument, which is none other than a convex bistoury, the price of which is only one peso in Manila. Surgeons

usually employ another bistoury with a blunt point, but we believe that this can be replaced by putting a small ball of wax on the point of the convex bistoury; and it is my opinion that in practice it is sufficient to cut the skin and the cellular tissue with a well-sharpened knife, reserving the bistoury with the ball of wax for the section of the peritoneum and the womb. If a razor is used, the handle should be firm and strong."

Judging from these statements, it appears that the medico-social influence of the missionary friars in the Philippines has been exceedingly important, especially in the field of obstetrics, and it is believed that with their evangelic advice, these priests dissipated the innumerable pagan superstitions relating to parturition, but, on the other hand, they sanctioned the use of many remedies utterly in conflict with common sense, some of which are to-day used by the lower classes. All of this is very excusable in these men, who were as full of the best desires and of love for their fellow-men as they were lacking in obstetrical knowledge. It is therefore not surprising that one still hears at the present time of some parturient to whom repulsive substances, such as dog urine, or mouse, horse or cow excrement have been administered.

Dr. Benito Valdez, of the faculty of the University of Santo Tomas, Manila, has recently told me of a parturient to whom a decoction of horse excrement was administered in order to facilitate labor, whereupon tetanus set in and the woman died. According to my informant, this case happened in Manila, approximately two years ago.

There are women who palliate the sufferings of childbirth by applying to the abdomen scapularies, images, medals, or to the feet, hands or other portions of the body relics of some famous saint venerated in the churches, or who drink, instead of urine or excrements, the miraculous water from Lourdes, accredited among pious people as an excellent medicine for facilitating parturition.

INFLUENCE OF THE CHINESE.

A very important factor which should be taken into consideration in this analytical study is the geographical proximity of the Celestial Empire to the Philippine Islands. Thousands of Chinese immigrants have invaded even the most remote parts of this Archipelago. One of the consequences of this immigration has been the introduction into this country of many superstitions originating in China which have become general among the Filipinos, and which have been strengthened by the arrival here of several Chinese physicians who practiced medicine among the natives according to Chinese usage. These so-called doctors acquired such influence that it is not an exaggeration to state that their queer therapeutic theories and practices are still followed by a portion of the population of the Philippine Islands.

While I was municipal physician in Carigara, Leyte, in the year

1904, I noticed that some of the inhabitants who [illegible] were treated [illegible] according to Chinese methods and with Chinese drugs. The latter were at times [illegible] in Chinese establishments. There are [illegible] in Manila [illegible] who [illegible] with pleasure the Chinaman who [illegible] and [illegible] fame and popularity [illegible] among families of the best social standing and position.

It goes without saying that the [illegible] originating in [illegible] influenced Philippine obstetrics, the [illegible] being [illegible] in regard to parturition, the exotic superstitions of the Asiatics [illegible] the autochthonous superstitions of the Malay race. I [illegible] it possible to make a comparative study of obstetrics in the Philippine Islands and in China and to ascertain the mutual relationship which may exist between the two. Historical documents which might shed light upon this interesting subject are, of course, lacking, but my own experience and the descriptions which I have secured from [illegible] me in giving some personal information on the subject of certain Philippine superstitions of Chinese origin. What I have learned is as follows:

When a woman has on the palm of the hand a transverse line completely crossing it, it is a sign that she will have difficult births and it is necessary that at the moment of parturition the line mentioned be covered with a handkerchief. Dr. Castaneda, expert in obstetrics in the Philippine Medical School, recently saw a woman in the district of Sampaloc who was about to give birth to a child and noticed that she had on each hand a silk handkerchief covering the lines on the palms.

Certain bricks of cylindrical form, *[illegible]*, are manufactured in this country especially for parturients. They are well heated and then applied to the abdomen of the patient for the purpose of expelling from the womb wind and cold, two atmospheric agents which, according to Chinese tradition, are mortal enemies of the parturient.

The patient is never given chicken broth, for as the chicken is winged and flies, it carries with it much wind which it might transmit to the patient and thus injure her.

Women who are menstruating are prohibited from entering the lying-in room because the effluvia of the former might be transmitted to the patient and give her fever or cause some other complication.

In cases of difficult parturition, the husband steps over the patient two or three times in order to cause delivery; and if this should not be sufficient, a pair of drawers which has been worn by the husband is tied to the woman's hair so that the smell of his father may cause the fœtus to emerge at once.

Where swooning occurs, and especially where there is hæmorrhage, the hair is bound in a tight knot, and the patient is not permitted to sit down, this to prevent the spirit from escaping from the body. A colleague told me of a terrible case resulting from this last superstition and witnessed by him in the Province of Ambos Camarines a few years ago. The wife of a Chinaman had a post partum hæmorrhage, caused by the retention of the placenta, and in order to stop the hæmorrhage, either the Chinaman himself or the midwife, or both, had the patient's coil of hair drawn very tight and by means of it they hung her from one of the beams of the house. The woman died in horrible convulsions while thus suspended.

In China the umbilical cord is not cut until the placenta has been expelled, for fear that the latter might rise, envelop the heart and kill the patient. Many Filipino midwives, influenced perhaps by this superstition, do not cut the umbilical cord until the placenta has been delivered, leaving the child sometimes for hours between the mother's thighs, covered with the sebaceous matter, meconium, amniotic fluid, blood and fæces. The placenta is cremated and then administered to the patient. The umbilical cord is burned, the ashes to be used as a remedy for stomach ache in children.

In China, when the parturient is in a very serious condition due to hæmorrhage, a chicken is killed, cut open and applied to the patient's breast to give her life. I have seen this done in the town of Ormoc, Leyte, when I was municipal physician in that settlement.

If the fœtus has coils of the cord around the neck, superstition has it that the boy will become a great man, as this condition recalls the Chinese mandarins and great dignataries who have bands covered with symbolic ornamental dragons wrapped around their bodies.

MODERN ADVANCES IN THE PHILIPPINES.

I wish here to render a tribute of consideration and affection to our colleagues who preceded us in the practice of medicine in these Islands and who planted in them the first milestones of rational obstetrics, according to the knowledge of that epoch. I do not allude particularly to the Spanish physicians, called *fisicos*, who, together with the troops and missions from Spain, landed each year from the famous Acapulco galleons, nor to those who came to this country between the years 1764 and 1869 with the expeditions organized at the port of Cadiz, sailing for Manila, by way of the Cape of Good Hope. These men formed such a small minority and had such scanty knowledge of obstetrics that their influence may well be disregarded in the evolution of this important branch of medicine in the Philippine Islands.

I wish to speak of the foreign, Spanish and Filipino physicians who, beginning in the years 1870, established themselves in Manila and the provincial capitals, shedding the first rays of the light of medical science on the chaotic state of affairs then prevailing. Among these pioneers of happy memory, I make special mention of the Englishmen Fullerton and the Burke brothers, the Germans Neizen and Koeniger, the Frenchman Permantier, the Portuguese Silva Magalhaes, the Spaniards Ginard, Marti, Meynet, Nalda, Pina, Torrejon, Sacristan, Mallen, Farinos and others who practiced medicine in this country. They are all deserving of gratitude and praise, because they contributed their grain of sand to the erection of the scientific edifice of obstetrics in the Philippine Islands.

The coöperation of Filipino physicians in the scientific labor already initiated was not long wanting after the creation in this capital of the faculty of medicine of the University of Santo Tomas. Beginning with the year 1867, diplomas to licentiates in medicine and surgery were issued every year to young men who scattered throughout the Archipelago to practice medicine, either as private physicians or in some public capacity under the former Spanish Government. Although, so far as parturition was concerned, it must be admitted that the clinical education given in the lecture rooms of the university was exceedingly deficient because of lack of a practical foundation, yet it is no more than just to acknowledge that, thanks to spontaneous efforts and extensive personal experience, many of the native physicians became expert obstetricians and contributed materially to the advancement of this branch of medical knowledge in the Philippines.

Prominent among these men is the figure of Dr. Felipe Zamora, who for many years and until the close of Spanish rule, was the best obstetrician of Manila and the adjacent provinces. More recently, excellent obstetricians have developed in the persons of Drs. Pablo Nalda and Manuel Madrigal, both deceased, and among our own contemporaries.

Another event connected with the history of obstetrics in the Philippine Islands was the establishment in 1879 of a school of midwives annexed to the University of Santo Tomas. The course consisted of four semesters. Fifty-six of the one hundred and thirteen pupils who were matriculated received the degree of midwife. The school suspended operations in the month of March, 1903. Nine years after its creation, by virtue of a royal order of February 28, 1888, the service of official midwives who might render gratuitous service to poor parturients was established for Manila and the provinces, but nearly all the provincial positions remained vacant, probably because of the lack of competent, qualified persons. There followed the establishment of the *inspección general de beneficiencia y sanidad,* by virtue of the royal order of September 10, 1888, to replace the old *subdelegación de medicina y farmacia,* which had existed since the year 1862. Later, there was founded the service of official physicians (*médicos titulares*) for the Archipelago, the latter being charged with the obligatory and gratuitous attendance of poor parturients within the municipal limits of Manila.

American sovereignty came in the year 1898 to replace that of Spain in the government and administration of these Isalnds, and after civil government had been established, the Board of Health was created in October, 1901. In December of the same year, the Board of Medical Examiners was constituted, charged with qualifying physicians, practitioners of medicine and midwives who wished to follow their profession in the Archipelago. Of the latter, thirty-three were registered, certainly a very insignificant number for the entire Philippine population. Thirty-one of these were from Manila, one from Iloilo, and one from Ilocos Sur, there being none from the other provinces. Eight of these thirty-three qualified midwives were appointed municipal midwives, to render, in conjunction with the municipal physicians, gratuitous services to parturients of the poor classes in the suburbs of Manila.

The Philippine Medical School was established by act of the Philippine Commission, December 1, 1905. It began operations July 1, 1907, and the chair of obstetrics was organized with its clinic in St. Paul's Hospital. Here several beds were reserved for poor parturients of this city. Similar action was taken by the San Juan de Dios Hospital, in consequence of the adoption of a new curriculum by the medical department of the Santo Tomas University.

ADVANCES IN THE USE OF INSTRUMENTS.

In the last two decades many obstetrical operations have been performed in the Philippines, such as the application of the forceps in its several varieties, versions by external, internal and mixed manipulation, the Cæsarian section on living patients, embryotomy, basiotripsy, provocation of premature labor, curettage, and perineorrhaphia of all kinds, with the exception of symphysiotomy and pubiotomy.

CONCLUSIONS.

It has clearly been demonstrated that in the Philippine Islands work has been going on for some time which tends to lead obstetrics into modern channels and to eradicate from the minds of the people the charlatanism, superstitions and irrational practices predominating in this branch of medicine. What has been the result of this scientific evolution? That it has been efficacious and useful to a large number of women belonging to the cultured families of this country who have at least realized that for confinements a physician should be called, is undisputed; but it has been negative in regard to the nameless mass of parturients of the lower classes who are completely given over to the illegal practitioners and midwives, with great danger to their own lives and to those of their new-born babes.

The services of a physician are, as a rule, dispensed with among the people of this stratum of society, even in the most serious cases of dystocia, and the patient is left to her fate. If a physician is sent for, he is almost always called after the moment has passed when a simple intervention on his part might have prevented the death of the mother, or of the child, or of both.

A few instances might be cited in this connection: Last September (1907) I received an urgent call to attend a parturient in Calle C, district of Malate. It was a very serious case of retention of the placenta and the woman, who had been delivered of a live child at 2 o'clock in the morning, was, five hours later, at 7 o'clock in the morning when I was summoned to her bedside, in the last moments of a terrible hæmorrhage. Intervention at that time was useless and the life of the patient could not be saved. The midwife was tranquil, believing that she had done her duty.

A little over a year ago I was called to the bedside of a woman in Calle Barbosa, district of Quiapo. This woman had been delivered of a live child at 10 o'clock in the evening. When I arrived at 2 o'clock the next morning, the placenta had not been expelled. A copious hæmorrhage had ensued, and while I was attempting to intervene, the patient began to collapse. The family subsequently informed me that a Chinese quack had acted as accoucher in the unfortunate delivery, but that he had disappeared upon my arrival.

Many other cases might be cited of parturients who have died of hæmorrhage, victims of the ignorance of the midwives. It is impossible to estimate the number of infants sacrificed by illegal practitioners who have folded their arms, content with a stupid temporizing in the frequent cases of *inertia uteri*, with the result that the child has died from prolonged detention in the vaginal canal, when a simple application of the forceps might have saved it. Among numerous cases of this kind I shall cite only one, which I witnessed in an interior street in the barrio of Santa Mesa at the beginning of the present year (1908). The woman was a multipara, her bladder had not been emptied for more than five hours, and the lack of uterine contractions had detained the child in the canal during the period of expulsion. When I sought to intervene with the forceps, the woman spontaneously gave birth to a beautiful and well-formed child which was born dead because of intrauterine asphyxia, and which could have been delivered alive if the midwife had had intelligence enough to call a physician at the proper time.

A large number of women die every year in the Philippines as a result of puerpal infections, not only because the midwives are ignorant of the most rudimentary conceptions of asepsis and antisepsis, but also because the rooms in which the confinements take place are absolutely lacking in hygienic conditions. In the miserable huts in which the poorer classes live, there are at times neither clean water nor soap with which to wash the hands, the work of attending a birth becoming a veritable sacrifice for the physician who finds himself compelled to labor under such conditions, but even under these circumstances it is as a rule useless to advise the patient of the absolute necessity of being taken to a hospital where she can have proper attention, such a proposal being acceded to by herself and her family only with the greatest reluctance.

The aversion which Filipino women have to entering hospitals is due principally to their great attachment to their homes, together with an excessive love, sometimes ridiculous and mistaken, for their families and relatives from whom they are seldom separated. They cling to this notion even at the cost of their lives. It is also certain that the improbable tales concerning the hospitals circulated by ignorant midwives and meddlesome practitioners of the neighborhood, add not a little to the fomenting of this spirit of aversion. For example, it is said among a certain class of people that all the parturients who go to the hospital are operated upon there, sometimes the abdomen being opened to extract the child. It is also told that parturients are placed in beds in proximity to those of dying patients and that they are compelled to witness the sadness and horrors of death and also that at midnight they hear the moans and laments of those seriously ill. These systematic detractors of hospital service also take pains to spread abroad a revised and exaggerated account of the bad administration of hospitals, especially with reference to alimentation and care.

As a result of all this, months and months pass during which the beds arranged for parturition in the hospitals are unoccupied by Filipino women. This is not only injurious to the parturients and their newborn infants, many of whom die without medical attendance, but is detrimental also to the students in obstetrics who do not and can not have an opportunity for practical study, being thus limited to being mere theorists in this branch of medicine so essentially practical and experiential.

However, it has been possible to correct this difficulty to a certain extent, by the appointment of two externs in obstetrics, charged with gratuitously attending poor women in Manila during childbirth at their homes, the students taking advantage of these opportunities for their clinical instruction. Without such recourse, which we owe to the initiative of the Philippine Medical School, students would finish their entire course without any practical experience in obstetrics. The difference between the number of births witnessed by students in the hospital and those which took place in private houses is instructive. In St. Paul's Hospital the students saw only two births during the semester from July 1 to December 31 of the year 1907, whereas during the same period they attended 76 births in private houses, classified as follows:

Normal births	47
Application of forceps	9
Versions, shoulder presentation	6
Placenta prævia	5
Breech presentation	4
Post-partum hæmorrhage	2
Puerpal eclampsia	2
Retention of the placenta	1
Total	76

Perineorrhaphia was performed in several instances.

The 76 births witnessed by students in the various districts of the city is a much greater number than the two which they saw in St. Paul's

Hospital; but, taking them all together, what do 76 births, during a period of six months, signify for a city the size of Manila? This insignificant total is an eloquent proof of the exceedingly small moral influence the physician exerts on Filipino women of the lower classes and, on the other hand, demonstrates the palpable preponderance of illegal practitioners and ignorant midwives, monopolizers of almost all the parturitions among the poor and ignorant women of the city. It is even true that the two externes in obstetrics have been compelled to avail themselves of the influence of illegal practitioners, by means of a wise policy of attraction, in order to attend confinements.

To eliminate the illegal practitioner is, for the moment, a problem difficult of solution, for of what advantage would an energetic campaign against them at present be when we lack competent midwives? If the externs in obstetrics are reduced to attending maternity cases in miserable, small habitations, it will be possible for them to take along not more than two or three students to each case, and for this purpose the students would have to confine themselves strictly to fortnightly turns. Lacking the most necessary things, at times even clean water, soap and towels for washing their hands, the students have been compelled by circumstances to perform operations in filthy beds in unsanitary places and in an unhygienic atmosphere, the lying-in room serving at the same time as bedchamber, kitchen and even workshop to an entire family!

In view of the data cited, it is not difficult to foresee that the obstetrical pavilion of the future hospital will be a failure unless energetic measures are resorted to and certain reforms adopted to bring the poor and ignorant women of this city there for confinement. One of the first steps, after the construction of this pavilion, should be the enactment of a law establishing a school of midwifery for the entire Archipelago, and, as a measure of attraction to induce the ignorant women of the city to go there for confinement, I propose that some of the most popular and best-known illegal practitioners from the several suburbs of Manila be admitted as students in that school. This suggestion, however strange it may seem, will give positive results in the field of practice, because eight or ten of these practitioners, matriculated as students and enabled to secure the degree of qualified midwife, would serve as excellent propagandists for attracting parturients to the obstetrical ward, much better than all theoretical means of doubtful success. In a word, the great prestige which some of these illegal practitioners now enjoy among the lower classes of Manila should be used, through a wise policy of attraction, to further the beneficent ends of scientific propaganda.

The defective midwifery service now existing in Manila should be organized by regulations rendering efficacious the gratuitous treatment of poor parturients. Nothing would serve this purpose better than to place the midwives under the immediate control of the externs in obstetrics, whose duty it would be to approve the birth certificates issued and to watch the obstetrical operations in their respective districts. The existing provisions regarding birth certificates should be strictly enforced in each instance, and for this purpose the curates and pastors of the churches in this capital should be required to comply with their obligation not to administer baptism to any child without the previous presentation of that document, in the same manner as death certificates are required in the case of funerals. If this should require an increase in the number of municipal midwives in Manila, then, for the sake of the poor, let the number be increased and, incidentally, the miserable pittance of 20 pesos per month which is now their stipend.

As soon as the obstetrical pavilion has been constructed, a circular should be sent to all the practicing physicians in this capital, courteously inviting them to bring to the clinic such maternity cases as they choose, leaving them complete liberty of action for intervention should they so require. In order to remove common prejudices and traditions, admission into the clinic should be permitted during the first year of its establishment, not alone to the parturient, but also to two or three of her nearest relatives, so that they may spread a knowledge of the undoubted advantages of confinement in the maternity ward as compared with those of private dwellings.

When the necessity for the establishment of a medical school for this Archipelago was discussed before the Philippine Commission, the theory was advanced that the project would result in a heavy burden on the Insular budget, it being more feasible and economical to send young Filipinos to America as Government students to study medicine. In making this objection, it was not taken into consideration that instead of an educational labor for the benefit of certain elements, a social labor within the Philippine Archipelago would be undertaken, involving the exceedingly important problem of infant mortality and of the practice in the Philippine Islands of obstetrics in accordance with modern methods and standards.

ILLUSTRATIONS.

Plates I–III. Conditions surrounding obstetrical practice in Manila among the poorer classes.

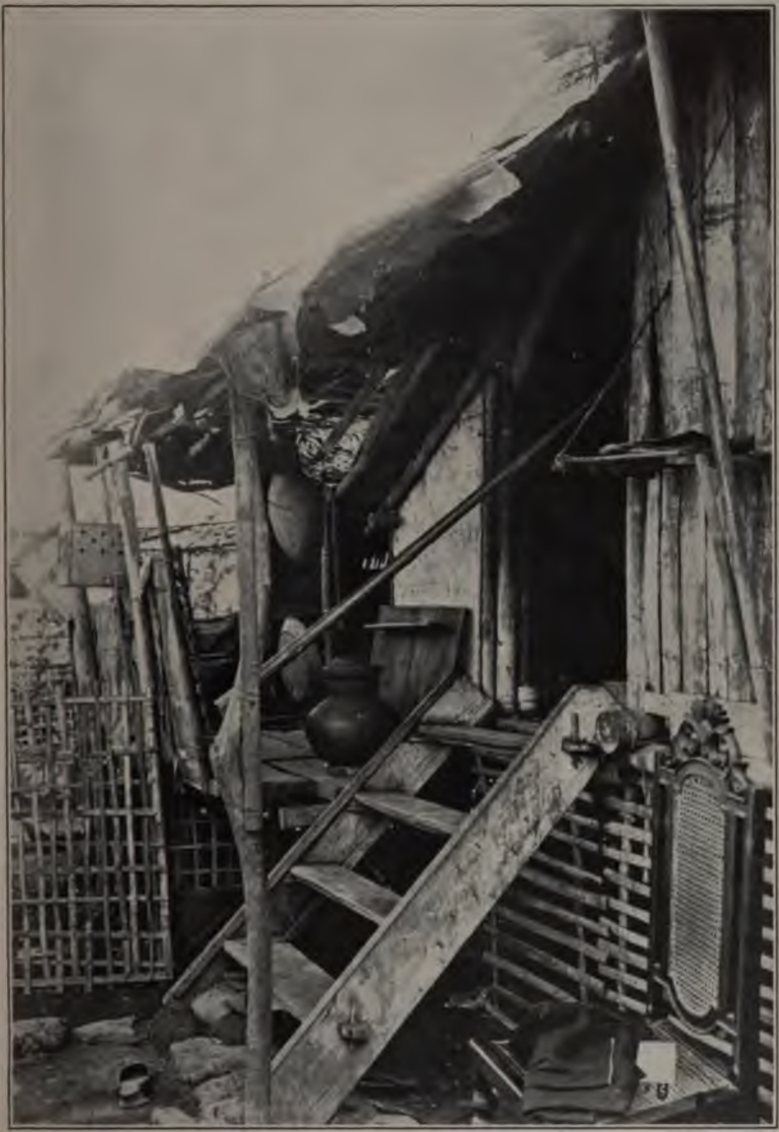

PLATE I.

PLATE II.

EDITORIAL.

DISCUSSIONS ON THE PAPERS OF DR. GARRISON AND DR. GILMAN.

(The papers of Dr. Garrison and Dr. Gilman were considered conjointly.)

Dr. Thomas W. Jackson, contract surgeon, United States Army, San Isidro, Nueva Ecija, P. I.—I was much interested in Dr. Garrison's paper and I have been much impressed with the statistics that have been compiled. My observations have been comparatively limited, but I believe that the conditions which Dr. Garrison has outlined for Bilibid Prison prevail throughout the provinces. They are of common occurrence, and from three to five distinct infections have often been noted among Filipino Scouts by many Army men. Indeed it is exceptional to find a solitary variety of worms in a native Scout. Two or more varieties are usually in association.

The effect of multiple *ascaris* infection was not mentioned by Dr. Garrison. By this I mean the occurrence of a large number of worms in the same individual and when the discussion closes I would like him to state the maximum number which has been observed in a single individual. I have already found in a child forty-eight round worms. The child was also infested with hookworms and amœbæ.

Dr. N. M. Saleeby, superintendent of the University Hospital, Manila.—One thing particularly interests me. A child in this city passed more than one hundred round worms, and I understand that a few days later it died. Does any one present know the death rate in these cases? I never investigated the subject, and I would be very glad if someone could enlighten me.

Dr. W. E. Musgrave, Biological Laboratory, Bureau of Science, professor of clinical medicine, Philippine Medical School, President of the Association.—It seems to me that these papers have brought out two prominent facts. In the first place, we find a large percentage of amœbic infection, both in diagnostic work (Garrison) and at autopsy (Gilman). This brings up the question of so much importance to the practicing physician of the means of diagnosis of amœbic infection of the bowel during the life of the patient. Dr. Gilman, in one hundred autopsies, found 54 cases with lesions of the colon, and it is altogether likely that at least 50 per cent of these were due to amœbæ. Dr. Garrison found that 25 per cent of stools of all people examined contained amœbæ, which is a smaller percentage than the findings in the autopsy room. These figures would indicate infestation without infection to be very rare and would justify the conclusion that we are all too prone to require the presence of blood and mucus in the stools before we state that actual amœbic ulceration of the bowel is present.

Dr. Henry S. Greenleaf, captain, United States Army.—Has anyone who has been making a study of these parasites found evidences of guinea worms? When I was in Mindanao I found a Moro pulling something out of a sore and I asked the interpreter what he was doing. The man pointed to a little worm which had been pulled out of the sore and from his description I thought it might be a guinea worm. Is this parasite common among the natives? I have not looked up the subject.

Dr. Musgrave.—I have been looking for a guinea worm for nine years.

Dr. Henry J. Nichols, first lieutenant, United States Army, Division Hospital, Manila.—I have had an opportunity to examine 400 soldiers doing active field duty, and 200 of these had amœbæ present in their stools. Twenty-five per cent had symptoms of dysentery, and of this 25 per cent only about one-half showed the presence of active amœbæ.

Dean C. Worcester, Secretary of the Interior, Philippine Commission, Manila.—I have seen evidence on the subject of amœbic infection and it leads me to believe that if an amœba is not pathogenic at one time, it may become so at another. It has been suggested, in connection with some of our diseases in the Philippines, that dysentery is a white man's disease, but I believe it is true that a very large percentage of the native inhabitants have dysentery in a chronic form, and this is one of the causes tending toward their disinclination to labor. I was very much interested in Dr. Garrison's paper. The Secretary of War, while in Manila, called my attention to the very satisfactory results which had attended the efforts made on such a large scale in Porto Rico to rid the inhabitants of intestinal parasitic worms and suggested that similar work might be necessary here. It would appear from Dr. Garrison's paper that this is not probable. However, it sticks in my memory that I have read a report of Dr. Heiser on conditions in Bilibid Prison which showed infection with parasitic worms to be quite general among the inmates of that institution and that when systematic measures were taken to rid the convicts of these parasites, the death rate from other causes was immediately and materially reduced, showing that the patients had been so weakened by the presence of these parasites that they had fallen ready victims to other diseases. I should like to know whether Dr. Heiser can confirm this statement.

Dr. Victor G. Heiser, Director of the Bureau of Health, Manila; professor of hygiene, Philippine Medical School.—I believe the mortality incidence in the Philippines to be very intimately associated with the intestinal parasites with which the inhabitants of these Islands are afflicted; we think we have statistics from Bilibid Prison that are fairly conclusive on this point. Several years ago the death rate was something over 200 per thousand. Ordinary sanitary methods were instituted—more air space was provided, drains were put in and other needful things done. These measures reduced the mortality to 60 per thousand, but this rate was still far in excess of what an institution of that character should have. We spent some six months examining into the various causes which might influence it. It finally occurred to us that intestinal parasites had some connection with the result, and I think the statistics will bear us out in our conclusions as they show that in each brigade of the 200 examined the mortality came down in a marked manner after the institution of remedial measures. When the prison was remodeled and the prisoners cured of their parasitic intestinal diseases, the mortality fell to 12 per thousand and has remained at that figure for the last six months. I think this result is one of the greatest triumphs of modern prophylactic medicine that has occurred in these Islands, and I believe that when the facts become known they will induce the laity to look with favor upon a campaign in these Islands for the elimination of intestinal parasites.

Dr. Philip E. Garrison, assistant surgeon, United States Navy; medical zoölogist, Biological Laboratory, Bureau of Science; associate professor of medical zoölogy in the Philippine Medical School.—We have reports of several hundred *Ascaris* removed from one individual. I think Dr. Musgrave recently recovered about 150 from a Filipino child at one treatment.

In our examinations a positive diagnosis of *Amœba* was made only when the moving organism was found in the stool.

A systematic clinical study of infected cases was not included in the purpose of my investigations and I am not prepared to offer any new information regarding the symptoms or pathology found in these infections. In considering the importance of intestinal worms as factors in either the death or sick rate of a community, the fact must be recognized that they play their most important rôle by predisposing to other diseases. Intestinal worms are rarely mentioned in mortality statistics, and it is exceedingly difficult to measure the relative participation in the death of the patient of the infection with intestinal worms which lowers the resistance of the host and the terminal infection which the mortality table recognizes as the immediate cause of death. The remarkable fall in the death rate at Bilibid following the institution of a systematic treatment for intestinal worms, of which Dr. Heiser has already spoken, is a striking contribution to our information on this very point, and if future records at the prison and the institution of similar measures in other communities should confirm the results which appear to have been accomplished there, even in a much less striking degree than the figures

Dr. Heiser has quoted would indicate, we shall be forced to the conclusion that intestinal worms, as predisposing factors to disease, are of greater importance from the viewpoint of the public health than the bacillary infections, such as tuberculosis, pneumonia, dysentery, etc., to which the weakened subject eventually succumbs.

With regard to the inquiry of the Secretary of War, of which Mr. Worcester has spoken, as to the need in the Philippines of a special, organized campaign against intestinal worms similar to that of the Anæmia Commission in Porto Rico, it would appear that in these Islands we have to deal with a condition different in several respects from that which confronted the health authorities in Porto Rico, the chief difference being the comparative rarity of severe manifestations of uncinariasis; and another, the greater population here. The results of the examinations at Bilibid indicate that not less than 5,000,000 of Filipinos are infested with intestinal worms and that these infections have a fairly even geographical distribution. To attempt to establish a helminthological clinic for these 5,000,000 of people would appear absolutely impracticable, even though we had ten times the means at hand that we now have, and took ten years for the campaign. Furthermore, such an effort would prove entirely unavailing without a practical revolution in certain sanitary conditions which prevail, as reinfection would constantly occur.

The one measure urgently demanded in the Philippines, in the light of our present knowledge of intestinal worms here, would appear to be the establishment of a system for the proper disposal of human excreta, thereby removing the almost exclusive channel by which these infections are spread. Until this is done, other measures would seem quite futile. We need only mention that in disposing of human excreta we eliminate one of the most dangerous channels for the dissemination of certain other prevailing diseases in addition to infections with intestinal worms. The methods to be employed and the question as to whether the work could be done better by a special commission or through existing organizations of the Government are subjects requiring special investigations.

REVIEW.

Hygiene and Public Health. By Louis C. Parkes, M. D., D. P. H., and Henry R. Kenwood, M. B., D. P. H. Third edition, with illustrations. Cloth. pp., xii+620. Price, $3 net. Philadelphia: P. Blackiston's Son & Co., 1907.

The third edition of this work shows evidence of having been thoroughly revised and considerable new matter has been introduced, so that it easily maintains the reputation of being one of the most practical treatises upon hygiene that is published in the English language.

Much of the useless theoretical matter found in works of this kind has been omitted. The authors' practical experience in dealing with public health matters in this regard is shown to excellent advantage.

It would seem that in a new work of this kind the means now so commonly used in the United States of cleaning houses by the vacuum method should have been mentioned.

Many of the data published in this work are derived from conditions as they obtain in Great Britain, and more particularly is this true with regard to legislation, so that because of this much of the value of the work is lost to the American student.

V. G. H.

PRIZES OFFERED BY THE INTERNATIONAL CONGRESS ON TUBERCULOSIS, TO BE HELD IN WASHINGTON, D. C., IN SEPTEMBER, 1908.

The central committee of the International Congress on Tuberculosis has announced the offer of the following prizes:

I. A prize of $1,000 is offered for the best evidence of effective work in the prevention or relief of tuberculosis by any voluntary association since the last International Congress in 1905. In addition to the prize of $1,000, two gold medals and three silver medals will be awarded. The prize and medals will be accompanied by diplomas or certificates of award.

Evidence is to include all forms of printed matter, educational leaflets, etc.; report showing increase of membership, organization, classes reached—such as labor unions, schools, churches, etc.; lectures given; influence in stimulating local boards of health, schools, dispensaries, hospitals for the care of tuberculosis; newspaper clippings of meetings held; methods of raising money; method of keeping accounts.

Each competitor must present a brief or report in printed form. No formal announcement of intention to compete is required.

II. A prize of $1,000 is offered for the best exhibit of an existing sanatorium for the treatment of curable cases of tuberculosis among the working classes. In addition to the prize of $1,000, two gold medals and three silver medals will be awarded. The prize and medals will be accompanied by diplomas or certificates of award.

The exhibit must show in detail construction, equipment, management, and results obtained. Each competitor must present a brief or report in printed form.

III. A prize of $1,000 is offered for the best exhibit of a furnished house, for a family or group of families of the working class, designed in the interest of the crusade against tuberculosis. In addition to the prize of $1,000, two gold medals and three silver medals will be awarded. The prize and medals will be accompanied by diplomas or certificates of award. This prize is designed to stimulate efforts toward securing a maximum of sunlight, ventilation, proper heating, and general sanitary arrangement for an inexpensive home. A model of house and furnishing is required. Each competitor must present a brief with drawings, specifications, estimates, etc., with an explanation of points of special excellence. Entry may be made under competitor's own name.

IV. A prize of $1,000 is offered for the best exhibit of a dispensary or kindred institution for the treatment of the tuberculous poor. In addition to the prize of $1,000, two gold medals and three silver medals will be awarded. The prize and medals will be accompanied by diplomas or certificates of award.

The exhibit must show in detail construction, equipment, management, and results obtained. Each competitor must present a brief or report in printed form.

V. A prize of $1,000 is offered for the best exhibit of a hospital for the treatment of advanced pulmonary tuberculosis. In addition to the prize of $1,000, two gold medals and three silver medals will be awarded. The prize and medals will be accompanied by diplomas or certificates of award.

The exhibit must show in detail construction, equipment, management, and results obtained. Each competitor must present a brief or report in printed form.

VI. The Hodgkins fund prize of $1,500 is offered by the Smithsonian Institution for the best treatise that may be submitted on "The Relation of Atmospheric Air to Tuberculosis."

The detailed definition of this prize may be obtained from the secretary-general of the International Congress or Secretary of Smithsonian Institution, Chas. D. Walcott.

VII. Prizes for educational leaflets.

A prize of $100 is offered for the best educational leaflet submitted in each of the seven classes defined below. In addition to the prize of $100, a gold medal and two silver medals will be awarded in each class. Each prize and medal will be accompanied by a diploma or certificate of award.

Competitors must be entered under assumed names.

A. For adults generally (not to exceed 1,000 words).

B. For teachers (not to exceed 2,000 words).

C. For mothers (not to exceed 1,000 words).

D. For indoor workers (not to exceed 1,000 words).

E. For dairy farmers (not to exceed 1,000 words).

F. For school children in grammer school grades (not to exceed 500 words).

In classes A, B, C, D, E, and F, brevity of statement without sacrifice of clearness will be of weight in awarding. All leaflets entered must be printed in the form they are designed to take.

G. Pictorial booklet for school children in primary grades and for the nursery.

Class G is designed to produce an artistic picture-book for children, extolling the value of fresh air, sunlight, cleanliness, etc., and showing contrasting conditions. "Slovenly Peter" has been suggested as a possible type. Entry may be made in the form of original designs without printing.

VIII. A gold medal and two silver medals are offered for the best exhibits sent in by any States of the United States, illustrating effective organization for the restriction of tuberculosis. Each medal will be accompanied by a diploma or certificate of award.

IX. A gold medal and two silver medals are offered for the best exhibits sent in by any State or country (the United States excluded), illustrating effective organization for the restriction of tuberculosis. Each medal will be accompanied by a diploma or certificate of award.

X. A gold medal and two silver medals are offered for each of the following exhibits; each medal will be accompanied by a diploma or certificate of award; wherever possible each competitor is required to file a brief or printed report:

A. For the best contribution to the pathological exhibit.

B. For the best exhibit of laws and ordinances in force June 1, 1908, for the prevention of tuberculosis by any State of the United States. Brief required.

C. For the best exhibit of laws and ordinances in force June 1, 1908, for the prevention of tuberculosis by any State or country (the United States excluded). Brief required.

D. For the best exhibit of laws and ordinances in force June 1, 1908, for the prevention of tuberculosis by any municipality in the world. Brief required.

E. For the society engaged in the crusade against tuberculosis having the largest membership in relation to population. Brief required.

F. For the plans which have been proven best for raising money for the crusade against tuberculosis. Brief required.

G. For the best exhibit of a passenger railway car in the interest of the crusade against tuberculosis. Brief required.

H. For the best plans for employment for arrested cases of tuberculosis. Brief required.

XI. Prizes of two gold medals and three silver medals will be awarded for the best exhibit of a workshop or factory in the interest of the crusade against tuberculosis. These medals will be accompanied by diplomas or certificates of award.

The exhibit must show in detail construction, equipment, management, and results obtained. Each competitor must present a brief or report in printed form.

The following constitute the committee on prizes: Dr. Charles J. Hatfield, Philadelphia (chairman); Dr. Thomas G. Ashton, Philadelphia (secretary); Dr. Edward R. Baldwin, Saranac Lake; Dr. Sherman G. Bonney, Denver; Dr. John L. Dawson, Charleston, S. C.; Dr. H. B. Favill, Chicago; Dr. John B. Hawes, 2d, Boston; Dr. H. D. Holton, Brattleboro; Dr. E. C. Levy, Richmond, Va.; Dr. Charles L. Minor, Asheville, N. C.; Dr. Estes Nichols, Augusta, Me.; Dr. M. J. Rosenau, Washington; Dr. J. Madison Taylor, Philadelphia; Dr. William S. Thayer, Baltimore; Dr. Louis M. Warfield, St. Louis.

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HEALTH CONDITIONS IN THE PHILIPPINES.[1]

By WILLIAM S. WASHBURN.[2]

The health conditions of any locality or country are only relative at best, and not absolute. The opposite state to that of health is disease, the principal causative factors of which are microörganisms, myriads of which surround us as unseen friends or foes. The maintenance of health appears to be dependent principally on an environment favorable to normal growth and development. It is now realized that the observance of the laws of personal, domestic, and public hygiene is the best protection against the invasion of the agencies of disease. Ignorance of these laws destroyed the health or lives of nearly 100,000 Spanish soldiers in Cuba in three years; and in the civil war, for every man killed by bullets there were two who died, and probably five whose health was permanently destroyed, by camp diseases which are now known to be preventable.

Instances of this character were formerly frequent and were not confined to military operations in the tropics; it is certain that such appalling death rates could have been greatly reduced by the intelligent application of modern sanitary measures. It would appear that the loss of Spain's tropical possessions is partly attributable to her failure to cope successfully with the lurking enemy, disease.

Under American administration, however, as early as 1903, the Surgeon-General of the United States Army was able to state that the admission rate in Cuba and Porto Rico of 1,300.24 per thousand and a death rate of only 6.72 per thousand indicated that the troops on those islands were as healthy as the Army at home in the United States during the decade 1888 to 1897, prior to the Spanish-American war, when sickness and mortality were the lowest recorded. It appears from the records that during the last five years of the decade, now nearly completed, of American occupation of the Philippines, the Army in the United States proper has reached an almost unprecedented state of health, measured by the death rate from all causes for the year 1906 of 5.28 and a rate from disease of 2.84, the lowest recorded, as against the death rate of 6.72 for all causes for the decade prior to the Spanish-American war, when no troops were in the Tropics. A death rate of 5.61 for 1905 was reported in the British army. The discharge, death, and total loss rates were lower in Cuba for the last three months of 1906—during which time American troops were again stationed in Cuba—than in any other country where American troops were serving, including the United States. Since the days of Spanish occupation yellow fever, the scourge of the Spanish army, has become nonexistent in Cuba and Porto Rico.

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[1] Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, February 29, 1908.

[2] Director of Civil Service, Philippine Islands.

It is my purpose to give a brief review of the advances made by the American Government toward better health conditions in the Philippines, and to indicate, though quite cursorily, the comparative health conditions at the present time, as shown by records and reports. In July, 1901, military government in the Philippines was formally succeeded by civil government. Until the spring of 1905 the health department was under the immediate charge of officers detailed from the Medical Department of the Army, and thereafter has been under the immediate direction of a medical officer of the United States Public Health and Marine-Hospital Service. The health phase of civil government responsibility has therefore been continuously under the immediate direction of men well trained in matters of public health and sanitation, who have carried on the work so well begun under the military régime and subsequently so faithfully supported in times of stress by the Medical Corps of the United States Army and the Public Health and Marine-Hospital Service in the fight against disease.

When the marines and troops were landed in Cavite and Manila in 1898, these places were described as being filthy in the extreme. Other cities and towns in the Archipelago were subsequently found to be also generally insanitary and unsuitable for occupation. For three years the work of sanitation was carried on under the military government, during which period the troops were for the most part engaged in active operations in the field, necessitating exposure frequently to all manner of disease and rendering difficult the observance of the laws of hygiene. Notwithstanding such adverse conditions, the chief surgeon of the Philippines Division reached the conclusion in July, 1900, that the relatively small percentage of sick in the army in the Philippines was largely due to the care and attention given by officers and men to sanitation; that increased appreciation on their part of its beneficial result to health and consequent increased efforts to carry out its rules with thoroughness, would result in a further diminution of the sick report; and that, roughly stated, one-half of the sickness in the Army could have been prevented if everybody had obeyed the sanitary recommendations of the medical officers.

In 1902 "The greatest noneffectiveness from disease and injury in the United States was reported in January, February, and March, during which the sick report of troops at home was larger than in the Pacific islands. In March the cholera epidemic began in Manila and the island rates began at once to increase, the greatest number of admissions and the highest monthly mortality being reported in July of that year." [3]

The value of the application of sanitary science and its influence on health conditions is shown by the decrease in the death rate and admissions to sick report per thousand among American troops in the Philippines from certain diseases, as follows:

Diseases.	1898.		1899.		1906.	
	Death rate.	Admissions.	Death rate.	Admissions.	Death rate.	Admissions.
Typhoid fever	7.58	68.21			0.00	8.88
Undetermined fevers	0.00	63.04			0.00	8.97
Malarial fevers			1.23	705.49	0.55	304.20
Tuberculosis			1.18	5.54	0.79	5.49
Diarrhœal diseases			6.11	748.59	0.40	174.55
Insanity	0.34	2.07			0.00	2.02
Venereal diseases					0.08	310.34

The statistics for the year 1907 show a marked further decrease for nearly all diseases in admission, death, and noneffective rates in the Philippines and in the number of sick invalided home from the Philippines for that year.

The mortality rate for the year 1906 of American troops in the Philippines was much lower than that of the native troops for every disease except tuberculosis, which caused 17.5 per cent of all American deaths from disease,[4] as against 6.66 per cent of all deaths from disease among the native troops, but the discharge rate for tuberculosis was only 27.10 per cent of the total discharges because of disease among the American troops as against 51.06 per cent for this infection among native troops, thus probably making the actual death rate from this disease, if those who died after discharge are included, greater among the native troops than among the American. One-seventh of the deaths in Manila are due to tuberculosis. The relative death rate because of tuberculosis in the Army serving in the United States was 0.78, as against 0.79 for American troops in the Philippines. The mortality rates of native troops in the Philippines were 2.58 per thousand from injuries and 8.93 from disease, 4.55 of which was due to beri-beri, Asiatic cholera, and malarial fever, all preventable, and 4.37 to other diseases.

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[3] Report of the Surgeon-General, United States Army, for year ended June 30, 1903.

[4] The statistics for 1906 on death and discharge rates of American troops serving in the Philippines include the number of those who were invalided to the United States, died, or were discharged.

For the year 1907 the mortality rate from all causes (diseases and injuries) of American troops in the Philippines was 5.92. The death rate among the native troops from disease was 5.06, while the rate among American troops from disease was only 3.61. The deaths among American troops in the Philippines from injuries were 39 per cent of their total mortality (fourteen men having been drowned, the same number as in the preceding year), the fatalities from disease being only 61 per cent of the total mortality. In 1906 over 50 per cent of the deaths among troops serving in the Philippines were due to injuries. Deaths from disease on account of service in the Philippines therefore appear to be approaching the low mortality rate from disease for the army in the United States.

For 1906 the admission to sick report rate for the army in the United States was 1,179.93 per thousand; in the Dutch army for 1903 the admission rate was 1,321 per thousand. The admission rate in the Philippines for the calendar year 1907 was 1,401. The average duration of each case in the Philippines was twelve days.

The following is an interesting comparative exhibit on the causes of ill health of American troops serving in the United States and in the Philippines: For 1906 in the Philippines the noneffective relative rates were, respectively, for venereal diseases 22.04, malarial fevers 6.39, diarrhœal diseases 5.49, and dengue 1.69—the noneffectiveness on account of venereal disease being nearly double the total of the other three named and more than double that of the army in the United States from this cause.

> "Of the 1,364 men discharged for disability in the United States, over 64 per cent were for disabilities not incurred in the line of duty, and of these, 51 per cent were contracted before enlistment. The principal causes of discharge, with the number for each cause, were: tuberculosis 149; venereal diseases 165; defective vision 141; defective hearing 90; and organic disease of the heart 71."[5]

Of 181 discharges of American troops serving in the Philippines in the year 1906, 38 were for causes existing *previous* to service in the Philippines, 22 or 15.4 per cent for causes *not* originating in the line of duty, 33 on account of *injuries* received in the line of duty, and 3 not in the line of duty, and the remaining, only 85, or 47 per cent of the total number discharged, from diseases incurred because of service in the Philippines and in the line of duty.

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[5] Report of the Surgeon-General, United States Army, for year ended June 30, 1907.

The chief surgeon of the Philippines Division, in his report covering 1907, states that "The number of days lost not incident to the service was 85,062 for the American troops," as against 156,267 days lost incident to the service, and in further comment says:

> "The very large proportion of total nonefficiency from sickness due to causes not incident to the service is the occasion of great solicitude to the authorities of the division, and active efforts are being made to reduce it. Could such be eliminated the health of the troops in the Archipelago would compare favorably with that of the army in the United States. Of these causes venereal diseases are by far the most important. * * * Eliminate malarial diseases and our admission rate per thousand per annum would be 1,192. Eliminate venereal diseases and the rate would be 1,178. Eliminate them both and the rate would be 969, or for sickness alone 764 per thousand, a rate unequaled in our territory except in Alaska. I should be glad to see this reached and have no doubt it can be if the suggested means are zealously employed."

Even by the strictest isolation of infected soldiers it will be difficult for the military authorities to reduce venereal disease so long as infected women near military posts are not also isolated. The responsibility for their isolation rests with the civil and not the military authorities.

Referring to malarial fever the Surgeon-General in his report issued in 1906 states: "This increase in a disease which is entirely preventable, and which last year caused seven deaths and an immense amount of noneffectiveness, should cause serious consideration as to the sufficiency of the preventive measures heretofore taken." The natives suffered more severely than the Americans from malarial fevers, but appeared to be less affected by diarrhœal diseases.

It was formerly thought that "natives of the Philippines eat and drink with comparative impunity articles of food and foul water, the use of which by white men is disastrous." They certainly have no such immunity to cholera, and the reports on autopsies and investigations made here by Gilman, of the Philippine Medical School and Bureau of Science, and by medical officers of the Army indicate that the natives do not possess the heretofore supposed immunity against intestinal parasitic diseases.

During the calendar year 1906 there were only forty-eight admissions and no deaths from typhoid fever among American soldiers in the Philippines. There was one death from this disease among the native troops. The death rate per thousand from this disease in the army in the United States was 0.28.

Comment is made upon an outbreak of beriberi among the Filipinos at the Louisiana Purchase Exposition, the only epidemic of this disease which has been reported in the United States. There were 59 cases, with four deaths, among the Filipinos. No other people were affected. The points of interest were the entire escape of 150 Filipino scouts, who were living in a model camp [illegible] and of 38 other Filipinos whose sanitary surroundings were good, while all of the cases occurred among the remaining 788 natives, who were for some time crowded into one small building under conditions of filth, bad ventilation, and extreme overcrowding. There were in this building twelve bunks for as many people in each room 10 by 12 feet. After the overcrowding and other insanitary conditions were removed, the disease ceased. Food as a factor could be excluded, because all the Filipinos—those who escaped entirely, like the Scouts, and those severely affected—had practically the same diet and a liberal one. A good quality of Louisiana rice was used by all.

As to the influence of race, the comparative records, all facts considered, do not seem to warrant the conclusion that colored and native troops are more resistant than white soldiers to the effects of tropical service. The death rates from all causes and from disease alone are highest among the Filipinos. While other rates are lower for the natives, it is to be borne in mind that American soldiers excused from any portion of their military duty, no matter how trivial the cause, are placed on sick report, which is not the case with native troops. "During the cholera epidemic in 1902 the admission and death rates for native troops greatly exceeded those of white soldiers, although the American negroes were the greatest sufferers of all." According to statistics the physique of the average colored soldier when enlisted is superior to that of the average white soldier.

The diseases more prevalent in the Philippines among the American troops in 1906, with the admission rate per thousand for each, are shown in the following comparative table:

Disease.	American troops.			Filipino troops.
	Total.	White.	Colored.	
Venereal diseases	310.34	309.17	322.27	63.25
Diarrhœa, including enteritis	130.69	130.63	131.96	95.40
Dengue	88.77	85.52	149.44	15.55
Dysentery	43.86	41.61	85.86	20.38
Dyspepsia	35.46	33.79	66.77	27.53
Alcoholism	30.37	31.57	7.95	.63
Articular rheumatism, acute and chronic	11.39	11.15	15.90	5.46
Diseases of the liver	6.54	6.73	3.18	1.89
Appendicitis	5.41	5.36	6.36	1.26
Measles	5.01	5.28	----------	.63
Typhoid fever	3.88	4.08	----------	.84
Heart disease, organic, including endocarditis and pericarditis	2.26	2.22	3.18	2.10
Insanity	2.02	2.13	----------	.63

The diseases more prevalent among the Filipino troops are shown in the following table:

Disease.	Filipino troops.	American troops.		
		Total.	White.	Colored.
Malarial fevers	393.15	304.20	318.10	44.52
Bronchitis, acute and chronic	67.03	27.30	25.95	52.46
Abscess, acute	44.76	35.95	35.06	52.47
Constipation	44.76	22.54	20.68	57.24
Dhobie itch	43.08	27.54	24.97	76.31
Beri-beri	36.98	.08	.09	
Fevers, undetermined	21.43	8.97	8.68	14.31
Conjunctivitis, acute	16.18	7.92	7.74	11.13
Tuberculosis	9.88	5.49	5.36	7.95
Cholera, Asiatic	2.73	.57	.60	
Pneumonia	1.68	.48	.51	

While "the rates for white soldiers serving in the Philippines exceeded those for colored troops under similar conditions in all cases except in point of admission to sick report, the respective admission, discharge, death, and noneffective rates being 1,675.18, 11.86, 9.42, and 63.66 for white troops, and 2,170.11, 2.71, 4.07, and 57.53 for the colored soldiers," it is noted that at the same time with respect to the troops serving in the United States "as usual, all rates for colored troops, except the death rate, were considerably lower than those for white soldiers. The admission, discharge for disability, death, and noneffective rates for colored troops from all causes were 884.32, 16.22, 10.68, and 37.35, respectively, compared with 1,199.16, 33.32, 4.94, and 47.55, the corresponding figures for white troops." The rates for admission, discharge, and constant noneffectiveness in the United States were better for colored than for white troops, but the death rate among the colored troops was nearly two and a half times that of white troops, being greater in almost all classes of diseases, especially so in diseases of the respiratory, digestive, and circulatory systems. "The rate for tuberculosis was more than four times as great, and for pneumonia more than tenfold. It is noticeable that while there were *twenty-two* deaths from drowning among the white troops, there were none among the colored."

This fact materially reduces the relative rate among white troops from disease.[6]

With reference to the influence of length of service of American troops in the Philippines, statistics for 1906 show the highest admission and noneffective rates during the first and second years of service, the lowest death rate during the second and third years of service, the lowest admission and noneffective rates during the third and fourth years of service, and the lowest discharge rates during the fourth and fifth years of service.

Considering the physical condition of recruits, the relatively high rates of admission, noneffectiveness, and deaths on account of injuries, the large percentage of diseases not incurred in the line of duty and not attributable to service, and the comparative immunity from certain contagious, infectious, and frequently uncontrollable diseases incident to residence in the United States, it does not appear that health conditions in the Philippines are *necessarily* unfavorable to American troops serving in the Philippines compared with service in the United States.

Let us now turn to a brief review of the comparative state of the general public health in the Philippines. Quoting from the first paragraph of the last annual report of the Director of Health: "The effect of the sanitary reforms which have been persistently carried out during the past few years commenced to show in a most concrete and substantial manner during the period covered by this report. The public health has been more satisfactory than at any time since American occupation of the Philippines, from which it is reasonable to infer that health conditions are better now than at any time for the past one hundred years or

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[6] The relative prevalence of certain special diseases among white and colored troops in the United States, with the admission rates per thousand for each, are shown in the following table:

Special diseases.	White.	Colored.
Venereal diseases	159.47	150.34
Tonsilitis	60.23	33.45
Bronchitis, acute and chronic	49.71	22.17
Diarrhœa, including enteritis	75.56	44.74
Malaria	52.20	20.56
Influenza	23.02	21.77
Muscular rheumatism and myalgia	31.93	39.50
Hæmorrhoids	7.89	16.53
Rheumatism, subacute and chronic	7.05	9.67
Measles	6.74	0.40
Dysentery	6.14	3.22
Tuberculosis	4.96	9.27
Typhoid fever	6.00	0.40
Pneumonia	2.20	4.43
Frostbite and freezing	0.71	4.43
Smallpox	.16	2.42

more. The death rate per thousand for the city of Manila has been reduced from 40.99 last year to 36.91; the rate for Americans being 5.59, which is a reduction of 3.75 over the previous year, and among Spaniards the rate dropped from 17.40 to 15.84."

It is expected that the death rate per thousand for the city of Manila for the current fiscal year will be reduced to 30 or below. For comparison, the death rates in the following cities and countries as shown by the last census and subsequent reports were as follows: *Cities*—Cairo, 1907, Egyptians 38.4, foreigners 27.4; Bombay, for three-fourths of the year 1903, Hindus 86.06, Mussulmen 77.21, Parsees 31.17, Europeans 16.73; Calcutta 37; Batavia 46; Madrid 32.1; Barcelona 30.7; Shreveport 45.5; Savannah 34.3; Nashville 39.7; St. Petersburg 31.1; Richmond 29.7; New Orleans 29.9; Washington, D. C., 22.8; Boston 20.1. *Countries*—Hungary 27; Austria 25; Italy 22.1; German Empire 21.5; France 21.1; United States 17.8; Switzerland 17.3.

At the time of American occupation of the Philippines, the principles of modern sanitary science were not applied. Habitations and other buildings were unclean and insanitary and frequently set in unhealthful surroundings. The people were not being instructed in personal and domestic hygiene. The mortality of infants under one year of age among the natives is shown to have exceeded "the combined mortality of Asiatic cholera, bubonic plague, smallpox, dysentery, malarial fever, typhoid fever, and beri-beri." What wonder that the mortality rates of natives were high and are still excessive?

The English-speaking population in Manila does not include the usual proportion of old and young persons, and some have returned to the homeland because of illness, which, however, from the best information obtainable, has rarely resulted in death. The death rate, 15.84, among the Spanish population in Manila, which is generally composed of the usual members of families, is lower than in the United States according to the last census and gives a fair basis of comparison of health conditions in Manila.

A striking illustration of the value of the persistent and thorough application of proper sanitary measures is the reduction of the mortality rate in Bilibid Prison from over 100 per thousand in 1905 to 20 per thousand toward the close of the fiscal year 1907. The number of deaths in Bilibid was formerly enormous, the number during the last fiscal year being less than one-half of that for the preceding year. Pneumonia has been epidemic in this institution.

Misleading articles[7] on the unhealthfulness of the Philippines written after returning to the United States by Doctor Louis H. Fales, a former physician-in-charge of the medical work in Bilibid Prison, appear to find their own refutation in the greatly reduced mortality rates under the application of proper sanitary measures. Unable[8] himself to apply successfully the principles of sanitary science, all his writings in medical journals in the United States have been colored by his own unhappy experiences in the Philippines.

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[7] The American Physician in the Philippine Civil Service. *Amer. Med.* (1905), **9**, 513. Tropical Neurasthenia and its Relation to Tropical Acclimation. ***Amer.*** *Journal Med. Sciences* (1907), **133**, 582.

During the last fiscal year there were treated in the Civil Hospital in the city of Manila "1,310 patients, of whom 818 were white people, 463 Filipinos, and 29 Chinese, Japanese, and other Asiatics. Of this number of patients only 29 deaths occurred, 3 being patients of outside physicians. As 8 of the deaths were those of patients brought to the hospital in a moribund condition, they may properly be excluded from the number of deaths in the institution. On this basis the death rate would be less than 1½ per cent of the cases treated."

The inadequacy and unsuitableness of the building used for several years past as a civil hospital are in part compensated for by the efficiency and devotion to duty of the medical and nursing staff of the hospital.

The last United States census reports show the average urban death rate in the United States as 18.6 and the rural death rate 15.4, or a difference of 3.2 in favor of the rural communities. Statistics are not available showing definitely the mortality rates in the Philippines outside of Manila. It is probable that any difference here is likewise in favor of the Archipelago outside of Manila, where practical application of sanitary measures has accomplished much through the hard work and guidance of the few available medical inspectors of the Bureau of Health, the Medical Corps of the Army at Army posts and the American teachers, several hundred in number, stationed in the *pueblos* throughout the Islands. No small measure of credit is due the teachers for their splendid, often heroic, work in combating disease and improving the sanitary conditions of the *pueblos* in which they have been stationed. Having the confidence of the people, they have been able to aid materially in applying the sanitary regulations of the Bureau of Health through instruction in schools and by giving wholesome advice to local authorities.

The health of American teachers of the Bureau of Education, distributed as they are all over the Archipelago, is probably a fair indication of the general health of English-speaking civilians in the Philippines who have avoided excesses and lived normal lives since coming to the Islands. There were during the past year approximately 800 American teachers in the Islands; there have been in former years upwards of 900, nearly one-third of whom have been women. In his last annual report the Director of Education states: "The statistics for the past year show an average of but six days' illness for each American teacher in the service. The general health of the force is excellent. So far as we have been able to determine, teachers enjoy on the average as good health here as in the United States, and our experience shows more conclusively every year that the teacher who takes reasonable care of himself has no cause to dread the effects of this climate."

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[8] It is proper to state that Dr. Fales was seriously handicapped as was his successor, in not being free to carry out sanitary measures properly. Since November 1, 1905, the Bureau of Health has had control and supervision of sanitation in prisons in the Philippines, the physician charged with the care of the health of prisoners at Bilibid being responsible to the Director of Health.

For the years 1902 to 1907, inclusive, the total number of American teachers who died in the Philippines or in the United States because of illness contracted in the Philippines is 60. The first considerable number of teachers, 600, arrived in the Islands in August, 1901, in which year one death occurred within a few days after arrival in the Islands, the cause being nephritis (probably chronic). There has been one death during the present calendar year from violence, making 62 in all. Sixteen deaths resulted from injuries or violence, the remaining 46 from diseases as follows: smallpox 11, cholera 9, dysentery 7, typhoid fever 3, tuberculosis 3, nephritis 3, one each from encephalitis, cerebral hæmorrhage, cerebral meningitis, pneumonia, diphtheria, abortion, heart disease, hepatic abscess, and two unknown. There were no deaths from malarial fever and diseases not incident to duty, which so seriously interfere with the health and efficiency of soldiers. Malarial fever was the cause, next to tuberculosis, of the highest death rate during the year 1906 among the American troops in the Philippines. Comparative freedom from these diseases accounts in a measure for the comparatively low sick and death rates among teachers.

The number of deaths by years was as follows: In 1901, one; 1902, sixteen; 1903, sixteen; 1904, nine; 1905, seven; 1906, seven; and 1907, five. The larger number of deaths during 1902 and 1903 is accounted for partly by the fact that teachers appointed prior to 1904 were not subjected to thorough physical examination before appointment, and partly by unfavorable conditions of living in the Philippines in the early years of American occupation. There were twenty deaths from smallpox and cholera, all of which save three from smallpox, occurred prior to 1904. Some teachers came to the Islands during 1901, 1902, and 1903 who were in ill health in the United States, hoping that the change of climate would be beneficial. It is a fact that the health of many of these was improved and maintained during their stay in the Islands.

These statistics are fairly indicative of the effectiveness of the application of prophylactic and hygienic measures and of the general health of Americans throughout the Islands. Deaths among the white population of the Philippines from smallpox and Asiatic cholera are now happily rare, and the illness and mortality from those obstinate diseases which prevail in the United States, such as pneumonia (the second in mortality rate in the United States), influenza, typhoid fever, diphtheria, measles, and scarlet fever is comparatively small.

With few exceptions the statistics of each succeeding year show a steady decrease throughout the Islands of the inroads made by dangerous communicable diseases.

Tuberculosis remains in the Philippines as well as in all other countries, the "great white plague" among all races of people, and takes front rank here among "dangerous communicable diseases." During the past year one-seventh of the deaths in Manila were due to this cause. Preventable with difficulty, it is far more serious in the Philippines than all of the so-called tropical diseases combined, including Asiatic cholera and bubonic plague. A bulletin on tuberculosis, prepared by the Bureau of Health, showing how the disease is communicated and urging prophylactic measures, has been widely distributed during the past year and is being taught in the public schools.

There appears to be a greater abatement among civilians than among soldiers of diseases due to intestinal parasites. Intestinal diseases due to parasites are positively known to be preventable by the exercise of sufficient care in eating and drinking. Fortunately, too, the great majority of cases yield to treatment. There is reason to believe that in the near future intestinal parasites, through the achievements of preventive medicine, may cease to be important factors in producing intestinal diseases. This accomplishment will be almost as much of a boon to the tropics as was the discovery of the means of preventing yellow fever.

Bubonic plague has disappeared from the Islands, no case having been reported for nearly two years. During the fiscal year ended June 30, 1903, there were 160 cases, for the fiscal year 1904, 94 cases, for the fiscal year 1905, 41 cases, and for the fiscal year 1906, 20 cases. Less fortunate are the Asiatic cities on the China Sea, where cases are frequently reported, and in India, where over 1,000,000 of the inhabitants are dying annually from this disease.

There is now in the Philippines much less smallpox than for many years past, a direct result of the thorough and extensive campaign of vaccination. Since the completion of the vaccination not a single death from smallpox has been reported in several provinces where formerly thousands died annually. During the last fiscal year 2,022,380 persons were vaccinated, an increase of 1,072,255 over the preceding year. Of three and one-half million persons vaccinated, one and one-third millions were reported as successful vaccinations. Not one case of loss of life or limb, and not one of serious infection has been reported. This record is conclusive evidence of the care with which vaccine is prepared at the Bureau of Science, and also, of the rigidness with which the instructions for performing vaccinations are carried out.

The working out of the leprosy problem has reached a stage which practically insures its final and complete solution. The segregating of the lepers from the rest of the inhabitants of the Philippines as a leper colony on the island of Culion has resulted in clearing all of the Islands, except a portion of Luzon, of persons known to the health authorities to be leprous and in already reducing the number from approximately 4,000 to somewhat more than 3,000. The constant withdrawal of leprous persons from among the inhabitants of the Islands reduces to a minimum the chances of infection. The presence of this loathsome disease, except an occasional case, must be practically limited by the lives of those assembled at Culion. Only one American and one European are known to have developed leprosy during the decade of American occupation of the Philippines.

While living in the Tropics is generally supposed to be detrimental to the health of white people as compared with people of the dark races, statistics show that in Manila, Bombay, Cairo, and other cities situated in the Tropics or subtropics there is a wide difference in favor of the white race between the death rates of foreigners and natives.

All the ills to which flesh is heir have been attributed in the Philippines to the tropical climate. There is no intention in this paper to discuss the climatic phase of health conditions in the Philippines. In a paper[9] on the relation between climate and health which I presented at a meeting of this association three years ago, among others the conclusion was reached that failures of people of the white race to live in the Tropics and maintain health, excluding localities characterized by excessive heat, high relative humidity, or unhealthful soil conditions, appear to have been due principally to nonobservance of the rules of personal, domestic, or public hygiene. Along this line the following simple health rules, published by the Bureau of Health on cards for general distribution, are quite to the point:

> It is easier to maintain good health in the tropics than in the United States, but in order to do so you should observe the following simple rules:
>
> 1. Be vaccinated to-day. The Bureau of Health will do it free of charge.
> 2. Never drink any water unless it has been either boiled or distilled, nor eat any raw vegetables. If you observe this rule carefully you will probably never contract dysentery, typhoid fever, cholera, or any other disease that originates in the intestines. Disregard of this rule is responsible for the return to the United States of over 50 per cent of the invalids who leave these Islands.
> 3. Fruit is wholesome, and may generally be eaten raw with impunity, provided it is of a kind that grows upon trees, well above the ground.
> 4. Avoid patent medicines. "Do not put drugs of which you know nothing into bodies of which you may know less."
> 5. Alcoholic stimulants are not necessary, the advice of "old resident" to the contrary notwithstanding.
> 6. Generally, disease-carrying mosquitoes fly only at night; therefore, always sleep under a good mosquito net.
> 7. Finally, observe the same hygienic rules that are applicable to temperate climates, including those of physical exercise.

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[9] *Am. Jour. Med. Sciences*, September (1905), **130**, **497**.

The marked lowering of the death rate in the United States, principally in cities, from 1890 to 1900, and in Cuba, Porto Rico, and Panama more recently, is invariably attributed to improvement in the water supply, in the method of disposal of sewage, to the elimination of cesspools and stagnant ponds, to proper drainage, to the destruction of or protection against disease-bearing mosquitoes, to a better milk supply, or to more healthful dwellings; in brief, to improved sanitary conditions.

> In Panama, "malaria has been so controlled that the sick rate of our total force in the month of April, 1907, was less than 17 per thousand; that is, out of every thousand men at work on the canal we had on an average during the month only 17 sick in hospitals each day. Among 6,000 Americans in the employ of the Commission, including some 1,200 American women and children, the families of these employees, we have but little sickness of any kind, and their general appearance is fully as vigorous and robust as that of the same number of people in the United States. During the year 1906 our death rate from disease among American employees was less than 4 per thousand. We believe that we have demonstrated that the tropical diseases, yellow fever and malaria, can be entirely controlled in the Canal Zone * * *. For the last sixteen months pneumonia has been very fatal among our negro laborers, being confined almost entirely to this class of labor. It affects the whites very seldom. * * * I am inclined to think that the advances made in recent years in tropical sanitation will have a much wider and more far-reaching effect than freeing Havana of yellow fever or enabling us to build the Panama Canal. I think the sanitarian can now show that any population coming into the tropics can protect itself against these two diseases by measures that are both simple and inexpensive; that with these two diseases eliminated life in the tropics for the Anglo-Saxon will be more healthful than in the temperate zone; that gradually, within the next two or three centuries, tropical countries, which offer a much greater return for man's labor than do the temperate zones, will be settled by the white races, and that again the centers of wealth, civilization, and population will be in the tropics, as they were in the dawn of man's history, rather than in the temperate zones, as at present."[10]

Great as is the work done by the United States in her other tropical possessions, a work of no less magnitude is being accomplished here. Whether in the Tropics, in the temperate zones, or in the arctic regions, the maintenance of health is ever largely dependent upon good hygiene and good sanitation. Any untoward influence of "tropical light" may apparently be easily obviated by the selection of underwear of the proper color, and an appropriate head covering, e. g., a cork helmet. These simple and inexpensive preventive measures appear to have been almost completely ignored by the American soldier and civilian in the Philippines.

What does the future promise in the way of further improvement in the health conditions in the Philippines? Within the coming year a modern sanitary sewerage system for the city of Manila and a system of water supply better in quality and quantity than the present one will have been completed; as will also the greatly-needed modern and well-equipped general hospital in Manila, the corner stone of which has already been laid. The facilities of this institution, together with the application of the results of the work of research in the field of scientific medicine conducted in the Bureau of Science, must tend greatly to alleviate human suffering from disease and to enable practical instruction to be given in the new medical school just established.

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[10] "Sanitation in the Canal Zone," an address to the graduating class, 1907, of the Cornell University Medical College; Gorgas, *J. Am. Med. Ass.* (1907), **49**, **6**.

Sanitary improvements are contemplated or under way in the larger towns of the Archipelago outside of Manila, and under the direction of the Bureau of Public Works the sinking of artesian wells in the provinces will be continued, thus cutting off a fruitful source of disease in rural communities by furnishing a better supply of drinking water.

The problem of reducing the very high infant mortality in the Philippines, due largely to improper food, seems about to be worked out through the more common use of pure milk, importations of which from Europe, Australia, and the United States have recently reached enormous proportions. Where drops of pure cows' milk were used by Filipinos in the earlier days of American occupation, quarts are now being employed. In actual application the "*gota de leche*" idea has been expanded into "*litro de leche.*"

The Pure Food and Drugs Act recently put into force in the Philippines will hereafter insure wholesome food, so important in any climate. The Director of Health is of the opinion that "from the character of the foods which have been rejected, it appears probable that much of the illness which has heretofore been ascribed to the tropical climate was probably due not so much to the effects of the climate as to the effects of the chemicals which the food products contained, prepared by foreign manufacturers for the use of the residents of tropical countries."

Hospitals and other institutions so essential to the well-being of a community and especially to those far from home, have recently been completed, are already under construction, or will be under way before the close of the year. St. Paul's Hospital, founded by the Archbishop of Manila, has been in operation nearly three years. There have been completed modern hospitals for the Navy at Cañacao, for the Army at Fort William McKinley and Baguio and at Army posts in other parts of the Archipelago; there are also the University General Hospital in Manila established by the Episcopal Church, and a large general hospital at Iloilo built by the Presbyterians. Two weeks hence the corner stone of the Methodist Hospital in Manila for women and children will be laid, while a new general hospital at Baguio is nearly completed. The churches have also opened several dispensaries in Manila and in the provinces, thus supplementing the work of the Bureau of Health in caring for the sick.

New club houses and gymnasia are being built in Manila and athletic fields developed. Excellent transportation facilities by railway and motor cars to Baguio and living accommodations there, render Baguio available this year to large numbers for the first time. An altitude of 5,000 feet, a temperature generally ranging from 12° to 22° C., pine forests, and a pure water supply, combine to make Benguet Province one of the most healthful places in the world. Fruits and vegetables of the temperate zone are being cultivated in this province. Many miles of first-class wagon roads have been constructed, a club house has been built, and golf links have been laid out.

Before the close of the coming year, with the masses of the christianized Filipinos of the Archipelago immune from smallpox, with the segregation of all lepers in the Islands at the Culion colony, with the completion of sanitary improvements of great magnitude now in progress, with the more complete extension of systematic scientific methods of sanitation to all parts of the Islands, and with the wider dissemination of sanitary knowledge among the people, it is hoped the battle waged under unusual difficulties to conquer disease in the Philippine Islands will have been partially won and some of the great problems in the realm of preventive medicine solved.

THE PREVENTION OF TROPICAL ABSCESS OF THE LIVER BY THE EARLY DIAGNOSIS AND TREATMENT OF THE PRESUPPURATIVE STAGE OF AMŒBIC HEPATITIS.[1]

By LEONARD ROGERS.[2]

During the last seven years I have enjoyed most exceptional opportunities for studying tropical abscess of the liver in Calcutta, and have now arrived at the conclusion that the disease can and should be prevented altogether in the great majority of cases. The following are, briefly, the steps by which I have reached this position.

In 1902[3] I published a paper on tropical or amœbic abscess of the liver and its relationship to amœbic dysentery, in which I gave tables to show that I had found living amœbæ in scrapings from the walls of 35 out of 37 consecutive liver abscesses, the two negative results being in those livers not examined until twelve or more days after the abscess had been opened and drained. Further, two-thirds of the abscesses, when first opened, were sterile as regards the presence of bacteria. Kruse and Pasquale had previously found amœbæ in only 6 out of 15 cases of liver abscess. I also showed that when both a clinical history and a post-mortem were available, in 90 per cent of the cases dysentery was found to be associated with the liver abscess, and in 95 per cent of these there was evidence that the dysentery preceded the formation of the abscess, which was always, in my experience, of the amœbic variety. I therefore concluded that the large tropical abscesses (as opposed to those due to suppuration in the portal veins or in the bile ducts) were always due to the *Amœba dysenteriæ* and were secondary to amœbic dysentery, although the latter might often be of a latent nature, giving rise to no typical dysenteric symptoms during life, but revealing itself in the shape of a few amœbic ulcers found post-mortem, usually high up in the large bowel in the cæcum or ascending colon.

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[1] Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, February 29, 1908.

[2] Professor of Pathology, Medical College, Calcutta.

[3] *Brit. Med. Journ.* (1902), 2, 844.

In a second paper, in 1903,[4] I gave an account of amœbic dysentery in India, illustrated by a colored plate, and discussed the mode of formation of amœbic abscess of the liver, and in 1905,[5] I dealt with the value of leucocytosis in the early diagnosis of amœbic abscess, and pointed out that, although occasionally an attack of acute hepatitis with leucocytosis may clear up without suppuration occurring, yet if such cases are followed up, sooner or later an abscess of the liver nearly always forms. I also narrated a case of acute hepatitis with leucocytosis, which cleared up under large doses of ipecacuanha. In 1906[6] I published an article on two cases of amœbic abscess of the liver successfully treated by aspiration and injection of the soluble acid quinine hydrochloride, without drainage, having found that the amœbæ in thick liver abscess pus could readily be killed by that drug in a strength of from 1 in 100 to 1 in 500, a method which has since proved effective in other hands, especially in early, deep-seated abscesses although it fails in many more advanced cases.

While on the lookout for the early stages of the disease for this line of treatment, I met with a number of cases of fever with leucocytosis and symptoms of acute hepatitis, in some of which aspiration failed to reveal any abscess; they yielded, however, very rapidly to full doses of ipecacuanha, thus showing that the increase of the leucocytes takes place before actual suppuration has set in and sometimes many days earlier. Last year (1907)[7] I published a series of such cases which were rapidly cut short in the presuppurative stage by the ipecacuanha treatment, which may be briefly summarized as follows:

> Fifteen cases were met with during twelve months in the Calcutta European General Hospital. In only three was there a clear history of dysentery or symptoms of it while in hospital, while these lost their fever and hepatitis after two to four days treatment with ipecacuanha, although they had previously suffered from fever for fifteen, thirty-four, and forty-one days respectively, and one had been aspirated for liver abscess with a negative result. In three more cases of acute hepatitis, without dysentery, not treated by ipecacuanha, the fever only subsided after from thirty-four to forty-nine days. In five similar cases treated with ipecacuanha the fever subsided in from one to six days, although it had previously persisted for from thirteen to fifty days, one patient having been aspirated with a negative result. Lastly, there were three cases of fever with no signs of either dysentery or hepatitis, other than very slight painless enlargement of the liver, but with leucocytosis of the same type as in the other cases, namely without very marked increase of the proportion of the polynuclears (usually from 70 to 80 per cent.) They had suffered from fever for thirty-five, forty-five, and fifty-three days, respectively, which ceased in from two to fifteen

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[4] *Brit. Med. Journ.* (1903), 1, 1315.

[5] *Ibid.* (1905), 2, 1291.

[6] *Ibid.* (1906), 1, 1397.

[7] *Practitioner* (1907), 78, 766; Fevers in the Tropics (Oxford Medical Publications) (1908).

days under ipecacuanha. This is the class of case in which a large, deep-seated, fibrous walled amœbic abscess of the liver forms very insidiously with irregular intermittent fever; it is commonly treated as malarial, and there are no obvious signs of hepatitis until a very late stage. Two of the above fifteen cases relapsed and returned to the hospital four and seven months later, respectively, with an amœbic abscess of the liver.

When dysentery is present and complicated by hepatitis, ipecacuanha is advised by Sir Patrick Manson and other authorities, but at the time the above paper was published I was unable to find any recent writer who recommended large doses of ipecacuanha for hepatitis when accompanied by dysentery, although several of the older authors in India, especially McClean and Norman Chevers, also strongly urged its use for this purpose. The considerations which led me regularly to adopt this treatment were the finding of dysentery associated with 90 per cent of tropical liver abscesses, and the fact mentioned above, that in many patients dying of liver abscess, without history or symptoms of dysentery, amœbic ulcers are found post-mortem in the upper part of the large bowel. I therefore regarded hepatitis, accompanied by leucocytosis, as an indication of the presence of latent amœbic ulceration of the large bowel, which indicated large doses of ipecacuanha for its cure. The results of this treatment, both of those cases mentioned above and of subsequent ones, have been so successful that during the last two years no instance of liver abscess has developed while the patient was in the European General Hospital, Calcutta, although a few patients have been admitted with an abscess already formed. A number of cases of such acute hepatitis in which an abscess was suspected (and in five instances sought for in vain by the aspirating needle) have cleared up entirely under the ipecacuanha treatment. The following three examples, which have occurred during the last two months, will serve to illustrate the value of this method of treatment.

CASE 1. *Very acute hepatitis following on dysentery, rapidly cured by ipecacuanha.*—A European male, aged 25, was admitted for dysentery of six weeks' duration, passing, without pain or straining, about six stools daily containing blood and mucus. He was treated with a castor oil mixture and with creolin enemas and the blood and mucus disappeared from the stools after ten days. Seven days later (September 11) he began to suffer pain in the hepatic region and in the right shoulder and his temperature, which had previously been slightly subnormal, began to rise. (See chart 1.) The liver dullness was not increased, extending from the sixth rib to the costal margin. The pains continued to be severe, and on the 13th the breath sounds were noted to be weak at the base of the right lung. Morphine was given for the pain, and quinine, 10 grains, three times a day for the fever. On the 15th there was profuse sweating, while the liver dullness reached up to the fifth rib. Five leeches over the liver relieved the pain somewhat. On the 16th, the right chest was observed to be moving less than the left, and on the 18th, X rays showed that the diaphragm on the right side was quite motionless, while there appeared to be a slight shadow in the right lobe of the liver.

Abscess of the liver was diagnosed. However, as there had been recent dysentery, which had not been treated by full doses of ipecacuanha, the physician in charge of the patient (who had over twenty years' experience with Indian diseases) agreed to use the ipecacuanha treatment for a short time before operating on the liver abscess, the existence of which he did not doubt. Thirty grains of the drug were given daily from the 19th to the 27th, with the result that the temperature steadily fell as shown in chart 1, and the signs of acute hepatitis simultaneously completely subsided. On the 20th, the pain over the liver and the sweating had both diminished, and the patient slept better. By the 21st, the pain had ceased over the liver, although it continued in a slight degree in the right shoulder for another day. On the 23d, the temperature was normal and there was no pain or sweating, and all suspicion of liver abscess had disappeared. The patient was kept in the hospital up to the 22d of November, but had no more signs of dysentery or hepatitis and gained weight steadily. There was no shadow of doubt in the minds of all who watched this patient that the ipecacuanha treatment averted suppuration in the liver.

CASE 2. *Dysentery followed by hepatitis with temporary recovery; very acute hepatitis successfully treated two and one-half months later with ipecacuanha.*—European male, aged 26, admitted August 20, 1907, with a history of dysentery eight months before, followed after three weeks by pain in the epigastrium. On admission there was slight enlargement of the liver with pain over it. Stools loose, but no blood or mucus; intermittent fever rising to 101° or 102° F. in the evenings. The diaphragm moved well, and there was only a slight increase of the leucocytes, with but 65 per cent of polynuclears. The symptoms of hepatitis subsided in three weeks under salines and quinine, and the patient left the hospital apparently well. He returned two and a half months later (November 26) having had fever every evening for the previous month and a half, with rigors at times and intermittent, sharp pain over the liver. His bowels had been constipated. He was now weak and thin. There was slight bulging in the hepatic region, without marked tenderness. The breath sounds at the right base were diminished, with a decrease of vocal fremitus and vocal resonance. The liver dullness extended from the fifth space to 3 inches below the costal margin in the nipple line. No œdema was present. The spleen was not enlarged. Under X rays the right half of the diaphragm was observed to be 2 inches higher than the left and scarcely moved, even with deep respiration, but there was no shadow. A blood count showed red corpuscles 3,570,000, white 15,000, ratio of white to red, 1 to 236; polynuclears 77, lymphocytes 23; large mononuclears 9 and eosinophiles 1 per cent.

Because of the acuteness of the symptoms and the fullness in the hepatic region, liver abscess was suspected, but it was determined to try the ipecacuanha treatment before operating, so 30 grains were given on the evening of the 27th, and 40 grains on the following four evenings. On the 28th and 29th the hepatic pain was distinctly less, and the patient could turn over on his right side, which he could not do before. On the 30th there was no pain or tenderness over the liver. On the 2nd of December his temperature remained normal for the first time, and a steady convalescence followed, the liver receding until it was only just felt beneath the costal margin. The ipecacuanha was continued in 30-grain doses at increasing intervals up to January 5, 1908, in order to guard against the possibility of a relapse, and the patient left the hospital apparently quite well on January 9. The rapid lessening of the pain, followed by the decline of the fever and decrease in the enlargement of the liver under the ipecacuanha was most striking in this case, and indicated that the treatment prevented suppuration of the liver.

Case 3. *Hepatitis, history or symptoms of dysentery rapidly subsiding under ipecacuanha treatment.*—European male, aged 51, admitted on December 3, 1907, for fever. He had been ill for two weeks with fever and pain in the right hypochondrium, with nausea and loss of appetite. No rigors, but the patient felt chilly at times, with sweats at night. The bowels were constipated. The liver extended 1 inch below the costal margin, and was very tender. Other organs normal. A blood count on the 11th showed 4,670,000 red corpuscles, 12,875 white, ratio of white to red 1 to 363, polynuclears 81, lymphocytes 12, large mononuclears 6, and eosinophiles 1 per cent.

Ipecacuanha was commenced on the 7th of December, 30 grains being given each evening. Two days later the temperature began to decline and reached normal on the 11th, after which there was only one rise on the 13th accompanied by a rigor, being possibly malarial in nature. On the 17th the liver had become reduced in size, being only just felt below the ribs, and the patient left the hospital apparently quite well on the 22d of December. (See chart 3.) This is an example of the less acute form of hepatitis, which drifts insidiously on into suppuration after weeks of intermittent fever. It is only one step further to the class already mentioned, in which there is no pain or tenderness over the liver, and the leucocytosis alone raises a suspicion as to the true nature of the case, which suspicion is confirmed by the chronic fever rapidly yielding to large doses of ipecacuanha.

METHODS OF GIVING IPECACUANHA.

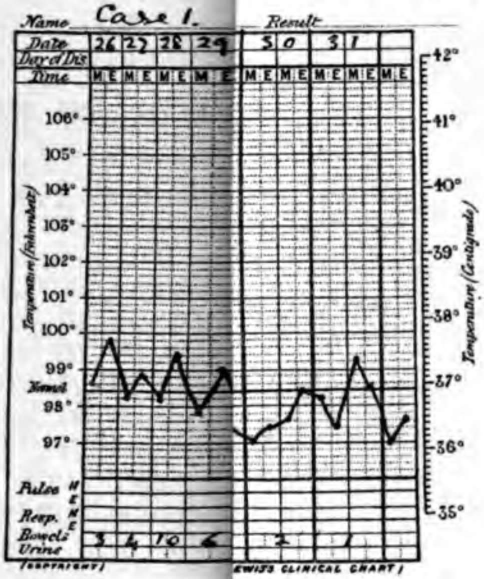
In giving large doses of ipecacuanha in amœbic dysentery and hepatitis, precautions must be taken to avoid vomiting, especially if it is possible that an abscess of the liver has already formed. The usual method is to give either tincture of opium or chloral hydrate some twenty minutes before the powdered ipecacuanha, no food or drink being given for several hours before and after the dose, which is best administered once a day in the evening. Recently I have had the drug put up in quantities of 5 grains in keratinized capsules, which are not dissolved until they reach the small intestines, and this has worked very well, no antecedent sedative being required. Dr. R. B. Grubbs, of the United States Army, has recently informed me that the same effect is produced by coating ipecacuanha pills with melted salol, but I have not yet had an opportunity of trying this method. From 30 to 60 grain doses of the drug have been used, but the smaller quantity appears to be sufficient. It should be continued for at least two weeks at increasing intervals, as two of my earlier cases, in which the ipecacuanha was discontinued as soon as the temperature fell, subsequently relapsed some months later, presumably owing to the latent amœbic ulcers not having been completely cured.

DURATION OF THE PRESUPPURATIVE STAGE OF AMŒBIC HEPATITIS.

There remains to be considered a very important question. What is the usual duration of the presuppurative stage of amœbic hepatitis, during which the ipecacuanha treatment will avert the formation of an abscess in the liver? An examination of my records during the last seven years has furnished the following data: Out of fifty-three native patients admitted to the hospital with liver abscess, often bulging through the thoracic or abdominal wall, 51 per cent gave a history of over two months' illness, and an additional 38 per cent, one of between one and two months; 9 per cent from two weeks to a month, and only 2 per cent under two weeks. Among 26 cases in Europeans there had been fever or hepatitis for over one month in 50 per cent, from two weeks to a month in 34.6, and of less than two weeks in only 13.4 per cent (4 cases of 9, 11, 7, 13 days respectively). It is clear from these figures that in the vast majority of instances there is ample time for the diagnosis by the blood examinations and for the ipecacuanha treatment during the presuppurative stage. Very rarely multiple abscesses may develop within a few days with extreme acuteness, yet I believe it is not too much to say that over 90 per cent of amœbic abscesses of the liver can and should be prevented by the methods described in this communication, and thus one of the greatest scourges of some tropical countries may be conquered.

ILLUSTRATIONS.

Charts 1, 2, and 3.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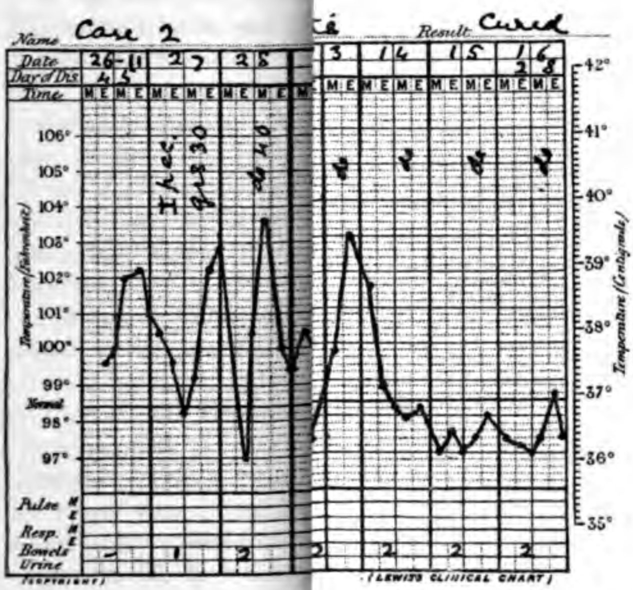
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FILARIASIS AND ELEPHANTIASIS IN SOUTHERN LUZON.[1]

By JAMES M. PHALEN and HENRY J. NICHOLS.[1]

I. INTRODUCTORY AND HISTORICAL.
II. ELEPHANTIASIS.
III. FILARIASIS.
IV. THE PARASITE.
V. MOSQUITOES.
VI. RELATIONSHIP OF FILARIA TO ELEPHANTIASIS.
VII. TREATMENT AND PROPHYLAXIS.
VIII. SUMMARY AND CONCLUSION.

I. INTRODUCTORY AND HISTORICAL.

It has been well known for years that filarial disease exists in the Philippine Islands, and the occurrence of its sequelæ, elephantiasis in its various phases also has been noted occasionally; but at the present time little is known concerning the frequency and distribution of these important maladies. A circular issued in 1901 from the office of the chief surgeon, Philippines Division, makes the first mention of filariasis in the Philippine Islands, as far as we are able to discover. This circular notes the discovery by Strong of a microfilaria in the blood of a European resident of Iloilo, the parasite being designated the *Filaria nocturna.*

Calvert, in 1902, performed an autopsy upon the body of a Filipino plague victim, and found groups of lymphatic varices in the pelvis and later an adult filaria in sections of the iliac lymphatics. This led him to examine the blood of a number of Filipino prisoners of war, with the result that he found two filarial infections out of four hundred and twenty-six persons examined. It is interesting to note that these two infections were in natives of the Province of Albay. The species of filarial embryo found was not given, but it had a nocturnal periodicity.

Doctors W. B. Wherry and J. R. McDill in May, 1906,[2] reported a case of hæmotochyluria in a Japanese girl in whose blood were found microfilariæ having a nocturnal periodicity, and which were considered to be *Microfilariæ bancrofti.* Ashburn and Craig, in 1906, described as a new blood filaria, *Filaria philippinensis,* and the same writers in 1907 published an excellent article relating to the development of this parasite in *Culex fatigans,* Wied.[3] Their observations were made upon five cases: one, a Visayan prisoner in Bilibid in Manila, and four, members of a Bicol company of Scouts, stationed at Imus, Cavite Province.

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[1] James M. Phalen, captain, Medical Corps, United States Army, and Henry J. Nichols, first lieutenant, Medical Corps, United States Army, constituting the United States Army Board for the Study of Tropical Diseases as they occur in the Philippine Islands.

[2] Publications of the Bureau of Government Laboratories, Manila, *Biological Laboratory* (1905), 31.

Dr. E. R. Whitmore, United States Army, reported recently before the Philippine Islands Medical Society the case of an American negro soldier from Parang, Mindanao, in whose blood were found microfilariæ morphologically identical with the *Filaria philippinensis,* but having a nocturnal periodicity. This man came from Charleston, South Carolina, and had been in the Philippines less than six months when the parasite was found by Dr. Eastman, United States Army, at Parang; hence there is a question as to the locality in which this infection occurred. The writers, in conjunction with Dr. E. C. Shattuck, reported before the same society a case of chylocele in a Bilibid prisoner, resident of Manila, whose blood showed the presence of an occasional microfilaria, answering the description of the *Filaria philippinensis* and apparently without periodicity. Dr. Shattuck has also given us the history of another Bilibid prisoner, a native of Camalig, Province of Albay, upon whom he operated for a hydrocele with great thickening of the scrotum and whose blood harbored a microfilaria of undetermined type. We have been told by medical officers of the United States Army of cases of filariasis occurring in various parts of the southern Islands, but no study has been made of them nor has the species in these cases been determined.

A number of cases of elephantiasis were observed among the natives of Sorsogon Province and the results of the investigations of these cases furnishes the basis of this paper. These patients were brought into the towns of Donsol, Bulan, and Sorsogon by the local health officers as suspected cases of leprosy during the segregation of lepers in this province. The presence of such a number of these cases suggested that the focus of a large amount of elephantiasis and consequently of filariasis might be found in this section of Luzon; and with this idea in view, a trip was made into this region, Camp Daraga constituting our headquarters.

The Provinces of Ambos Camarines, Albay, and Sorsogon occupy the most southern and eastern part of Luzon. They form a narrow strip with a high, central ridge broken by volcanic peaks, such as Bulasan, Mayon and Isarog, from which the land slopes gradually to the Mindoro Sea on one side and the Pacific Ocean on the other. The land is high and well drained except along the coast. Short, rapid streams, with deeply worn courses abound everywhere. The annual rainfall is higher than in almost any other section of the Archipelago, the northeast and southwest monsoons bringing rains to a large part of this section. Vegetation is luxuriant, even for the Tropics. This is the greatest hemp district on the Island, the greater part of the land being given over to the cultivation of the abacá plant. Altogether it is difficult to find anywhere in the Islands a prettier or a more prosperous region than this country of the Bicols.

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[3] *This Journal* (1907), 2, 106.

II. ELEPHANTIASIS.

This malady is well known among the native population by the name of *titibac*. Practically the entire laboring class of this section work at some time or other with hemp (abacá), hence it is not surprising that they should attribute the disease to the effect of that plant. There seems to be a diversity of opinion as to the way in which the plant affects the individual. Some believe that elephantiasis is due to the direct action of the sap of the abacá upon the skin, but the more prevalent idea connects the disease with the strain upon the legs incident to hemp stripping and followed by getting the feet wet. Many of the women as well as the men are workers in hemp, but those who have never engaged in work of this kind usually attribute the disease to the strain of working a loom, one of which is found in every home. Another cause of the disease is said to be getting the feet wet during menstruation. The typical history given by the patients, however, is that of a day's hard work at hemp stripping and wading, while still warm, through some stream on their way home. The following day brings on an attack, which in different towns, is variously called *sorip, ubag* or *culibra;* during the attack the leg becomes swollen, red, and painful.[4] There is also fever and loss of appetite. With the subsidence of fever and pain, some swelling of the leg persists. In many instances the history of but one such attack can be elicited, while in many cases, especially in the aged, the enlargement seems to have come on gradually without acute symptoms. One patient was observed during such an attack. This was a woman aged 28, a resident of Daraga, Albay Province, who, ten months before, suffered her primary attack, which left the left leg markedly swollen. There was also some swelling and induration of the lower part of the thigh. When seen she had a temperature of 37°.5 C. (103°.4 F.), and complained of headache; the left leg and thigh were hot and tense to the touch and tender on pressure; large, scattered erysipelatoid patches were situated over the inner side of both leg and thigh. The femoral glands were also swollen and tender. As this patient lived a long distance from the post of Daraga, the further course of the disease could not be observed.

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[4] Probably because of the distribution of the mosquito carriers of filaria, these infections do not seem to be as numerous along the coast as in the higher lands of the interior. A European merchant of Legaspi explained the fact of there being no elephantiasis in that town by the statement that Legaspi was not in the hemp district. One man, living near the coast, attributed his elephantiasis to pulling *bejuco* (rattan), which necessitated his wading in the water.

Thirty-four well marked cases of elephantoid disease were seen. Of this number, nineteen were males and fifteen females. The ages varied from 12 to 80 years, a large proportion being above 50 years of age. The average age at which the disease first made its appearance was somewhat between 30 and 35 years. The parts affected, either alone or in association with other parts, were as follows: Both lower extremities, 13 cases or 36.4 per cent; one lower extremity, 20 cases or 58.8 per cent; one upper extremity, 2 cases or 5.8 per cent; scrotum, 11 cases or nearly 58 per cent of the males; and groin glands, 3 cases or nearly 8 per cent of the total number.

The lower extremities.—Nearly every case of elephantoid disease observed had some involvement of either one or both of the lower extremities. The degree of enlargement varied from the most moderate grade up to instances where the calf exceeded 25 inches in circumference. (Plate I, fig. 1.) Usually, the foot and leg were involved, but in a few cases only the foot and ankle, and in others the foot, leg, and thigh. The skin was usually tense and glossy over the enlargement of the leg and thigh, while it was rough and warty around the ankle and over the foot. In one case large tuberose swellings were situated entirely over the ankle and foot. (Plate I, fig. 1.) Increased pigmentation was usual, the glandular structures were atrophied, the hair thinned and roughened or absent, the nails rough, thick, and brittle. Sensation was diminished. Deep pressure, long continued, produced pitting, but the under tissues were felt to be hard and indurated. The subcutaneous tissues were seen to be increased in volume. At the ankle the skin was thrown into folds, deep fissures intervening, permitting a small range of motion to the joint. The knee joint, when the thigh was involved, was less affected and in the cases observed, movement was not interfered with. Despite the hypertrophy of these parts, the vitality appeared to be good, ulceration or abscess was not observed in any of these cases.

The cases of enlargement of the upper extremity were of moderate degree, and presented no features of importance.

The scrotum.—Somewhat over half of the males affected with elephantoid disease had some involvement of the scrotum. Usually, the enlargement was of a moderate degree, the size of a coconut or a little larger. The largest seen hung to the level of the patient's knees, was 30 inches in circumference and weighed approximately 30 pounds. No case of lymph scrotum as described by Manson or Scheube was observed, the lesion being invariably an elephantiasis. The skin was rough and coarse and the subjacent tissues enormously thickened. The penis was always retracted to some degree, and in the extreme cases (Plate I, fig. 2.) was lost sight of in the folds of the scrotum, the urine reaching the surface along a channel formed by skin.

Fluctuation could be distinguished in a large proportion of these cases, but frequently the thickening of the subcutaneous tissues was so extreme that the fluid could not be reached with an ordinary needle. This fluid, when obtained, may be milky or more commonly of a clear, straw color. In our cases the amount obtained was about 350 to 500 cubic centimeters and was highly albuminous. Filarial embryos were usually found in great numbers in this fluid.

Glands of the groin.—Although some enlargement of the glands of the groin was present in nearly every instance, but three cases were observed, answering the classical description of varicose groin glands. The patients were all men, 40 to 50 years old, and in each case other manifestations of filarial disease coëxisted. The glands involved were the superficial inguinal, lying above and parallel to Poupart's ligament, and the disease was bilateral in all of the cases observed. The swelling was larger than that of the ordinary bubo, and was hard, without fluctuation, and could be felt to be separated into a small number of detachable masses. It was painless and not tender to the touch. The subjacent skin was freely movable over the mass, which, however, was firmly fixed to the deeper tissues. Attempts were made to obtain fluid from these glandular masses with a hypodermic needle, but with the exception of a little blood and serum nothing could be withdrawn. No history of an acute inflammation in these glands could be obtained from any of the patients, except that during the attacks of lymphangitis in the legs, they were tender.

III. FILARIASIS.

Examination of the blood of these patients showed the presence of filarial embryos in but three instances. However, it was possible to make examinations extending over the twenty-four hours of the day in only seven of the number. In the other twenty-seven only specimens taken during the daytime could be obtained. Two specimens out of the seven examined, both day and night, had filarial embryos in their blood, while of the twenty-seven whose blood was examined only during the day, one showed the parasite.

A number of examinations were made upon the general population. Of a total of eighty persons examined, filarial parasites were found in the blood of eleven; out of thirty-seven prisoners in the provincial jail at Albay, nine showed the presence of filarial embryos in blood specimens taken at 10 o'clock at night. These were all short-term prisoners from different towns in the Province of Albay. Out of 93 members of the Thirty-second Company, Philippine Scouts, recruited from Bicol Provinces, blood specimens from whom were sent to us by Dr. Warriner, United States Army, nine, or 9.6 per cent were found to be infected.

IV. THE PARASITE.

The filarial embryos present in the blood of these patients were studied both in fresh preparations and by appropriate staining. The parasites, so far as we could make out, were of one variety; the chief features are as follows:

Motility.—In fresh specimens of the infected blood, the parasite was observed to have the usual wriggling, lashing movements, which changed its position, but which could not be called progressive as the movement was accomplished in no orderly manner. It was only by observing that the lashing movements eventually removed the parasite from the field of the microscope that any change of position could be determined.

Size.—The average length of the microfilaria in the fresh preparation is about 0.300 millimeter and in stained specimens about 0.270 millimeter. The average diameter is 0.007 millimeter.

Head.—The head is smooth and hemispherical, surrounded by a notched prepuce having five or six notches. Upon the anterior end of the head is a slightly refractive spot, from which at times is projected forward a short, needle-like process, which is as quickly withdrawn.

Tail.—The tail slopes gradually to a very fine point.

Body.—The body is cylindrical for the greater part of its length, and is marked by the anterior V spot, the central viscus and the posterior V spot.

The anterior V spot is a triangular area, highly refractive, occupying one side of the worm, 0.090 millimeter, on an average, from the anterior extremity.

The central viscus is situated in the posterior part of the central third of the body. It is granular in appearance, but upon focussing carefully a convoluted tube can be seen to occupy this granular mass. The length of the central viscus is about 0.040 millimeter.

Posterior V spot.—We were unable to do more than to make out the presence of such an organ, and were not able to distinguish any details of the structure.

By appropriate staining, a granular, central column is shown occupying the center of the entire length of the worm. This column is broken by occasional unstained areas. The only one which showed at all constantly was situated in front of the anterior V spot, from 0.055 to 0.060 millimeter from the anterior extremity.

The stains which gave the best results in the embryo were gentian violet, Bismarck brown and hæmatoxylin in weak solutions, Borrell's blue and polychrome methylene blue. The latter two, mixed with glycerin, each gave excellent results, not only staining the parasite, but preserving its size and appearance as in fresh specimens.

Sheath.—The embryo has a sheath which exceeds the length of its occupant by one-third to one-half of the latter, but which appears to be, tightly applied to the body laterally. Ordinarily it may be observed as a fine flagellum at either end of the embryo, but at times may be seen as a flattened band. Stained specimens show the size and shape of the sheath very well. No movement of the filaria within the sheath has been observed.

Periodicity.—While it was not possible to obtain day and night specimens of blood from all of the cases, a sufficient number were examined at different hours to show that a nocturnal periodicity was the rule. The following table shows the result of the examination of a daylight and a night specimen from all patients from whom we were able to obtain them at both times:

Patient No.	10 p. m.	10 a. m.	Patient No.	10 p. m.	10 a. m.
1	21	0	6	73	0
2	124	1	7	8	1
3	4	0	8	9	0
4	22	0	9	3	0
5	7	0	10	28	0

Method.—In taking these specimens, four rather large drops of blood were placed close together on a slide. They were then run together with a needle, forming a thick, square smear. After being allowed to dry thoroughly, the hæmoglobin was dissolved by placing the slides face downward in a shallow dish of water with each end resting upon a glass rod. When the hæmoglobin was discharged, which took but a few minutes, the slides were quickly run over with a low-power objective while still wet and without staining, the filarial embryo catching the eye immediately as it came into the field.

Blood counts.—Differential leucocyte counts were made upon a number of the subjects of elephantiasis to determine the degree of eosinophilia present. The counts showed an average of little less than five per cent, the highest being 8.5 per cent and the lowest 1 per cent. The other leucocytes were present in the normal proportion. The percentage of eosinophiles in filarial disease is usually given higher than this, but here we are dealing with many old cases from whose blood the filaria had long since disappeared, and it is not to be expected that as high an average of eosinophilia would be found as in more recent infections.

V. MOSQUITOES.

The following is the list of the mosquitoes reported from the post of Camp Daraga, the identification having been made by Miss Ludlow of the laboratory of the Surgeon-General, United States Army: *Mansonia uniformis* Theob., *Stegomyia fasciata persistans* Banks, *Uranotænia cæruleocephala lateralis* Ludlow, *Culex microannulatus* Theob., *Culex gelidus* Theob., var. *cuneatus, Myzorhynchus barbirostris* V. d. W., and *Myzorhynchus vanus* Walk., the latter two belonging to the Anophelinæ. With the exception of *Culex microannulatus* none of the mosquitoes of this list, so far as we know, have been identified as filaria carriers, though with the limited knowledge that we have, none of these species can with certainty be acquitted of the charge of spreading the disease.

VI. RELATIONSHIP OF FILARIA TO ELEPHANTIASIS.

Prout, at a recent meeting of the London Society of Tropical Medicine, presented a paper in which the theory of filarial infection as the essential cause of elephantoid disease was brought into question. He gave it as his opinion that a majority, if not all the cases of elephantiasis, in the Tropics as in temperate regions, are due to an ordinary streptococcic lymphangitis, aggravated by lack of attention, and he brings forward a formidable array of evidence in support of his position. To be sure, the arguments in support of the relationship between the *Microfilaria bancrofti* and elephantoid disease are few in number: namely, that the *Filaria bancrofti* is a parasite of the lymphatic vessels, and elephantiasis is a disease of the same vessels, and also that the geographical distribution of elephantiasis and filariasis coincide. Our own investigations add their mite of evidence to the generally accepted view that elephantoid disease is directly due to filarial infection. Although our examinations for filariasis have not been very numerous, nevertheless they indicate a higher percentage of infection for the Bicol provinces than has been shown for any other part of the Islands, with probably the exception of the Davao district in Mindanao, and in no other portion of the Archipelago has elephantiasis been encountered in any like degree. Other writers have also observed that the subjects of elephantiasis showed a lesser percentage of filarial infection than the general population. Sir Patrick Manson speaks of finding but one filarial infection among fourteen subjects of elephantiasis, and twenty among seventy-four persons not so affected, all the specimens coming from the same locality. He explains this phenomenon by the view that the production of elephantoid disease results from some injury to the adult filaria, causing her to evacuate her eggs instead of the living embryos into the lymphatic vessels. The eggs, being of much greater diameter than the embryo, can not pass through the lymphatics, but obstruct them instead. Then, either because of the death of the adult worm, or of the clogged condition of the lymphatics, filarial embryos are no longer able to get into the circulation.

VII. TREATMENT AND PROPHYLAXIS.

The household remedies of a people are always of interest to the physician. The popular remedy for acute attacks of the lymphangitis is the leaf of an indigenous plant which the natives call *anonang* (*Cordia blancoi* Vid.). This is first bruised and mixed with salt and then applied to the affected parts. *Azafran* (*Curcuma longa* Linn.), the juice of the root of a local plant, is also commonly used as a local application. Multiple parallel incisions through the skin are also employed for the relief of the swelling, a penknife being used for the operation. The only treatment of elephantiasis observed by us was that of a cord tied around the leg to prevent the swelling advancing higher. (Plate I, fig. 2.) However, quite as futile as the string have been the numerous parasiticidal drugs that have been used from time to time for the treatment of filariasis: thymol, quinine, boric and benzoic acid, sodium benzoate, and numerous others. Scheube records a cure with picric-nitrate of potassium, and reports another by Flint, who used methylene blue for the purpose.

Rest, elevation of the parts, and compression by means of bandages are the means most frequently employed for the treatment of elephantiasis of the extremities. Hot baths and local applications of mercurial ointment are also used with benefit. Surgical measures, such as excision of longitudinal strips of skin, and the ligation and compression of the arteries supplying the part have been proposed, but are of no value and are dangerous as well. The combination of rest, elevation and compression together with injections of thiosinamin has been quite successfully employed by Castellani in Colombo, who, in 1907, reported the result of such treatment on a number of cases. His method of treatment[5] is to keep the patient in bed for a week, in the meantime bandaging the affected part with flannel or rubber bandages, and using massage twice daily. The thiosinamin solution is then injected into different parts of the affected area, 2 cubic centimeters of the solution every day or every other day. After the injections, the part is again tightly bandaged. A month or more of this treatment usually suffices greatly to reduce the affected parts, and the use of a puttee or elastic stocking will keep the swelling down. This treatment is only palliative and the enlargement will return if all compression is removed. The treatment of elephantoid disease of the scrotum is largely surgical and will not be considered here.

The prevention of such diseases is of great interest to us. The only way to insure protection against filarial disease in an endemic locality is by the methods of prophylaxis, based upon our knowledge of the life-history of the parasite. The anti-mosquito measures taken to insure protection from malaria will be equally efficient in warding off filarial disease. In addition, the blood of native servants should be examined after 10 o'clock at night for the presence of filarial embryos, and no person harboring the parasite should be employed about the house. Sporadic cases reported from widely separated sections indicate that these precautions would not be out of place anywhere in the Islands. In the military service it would be advisable to have not only the house servants examined, but also all natives employed in any capacity about the posts, and to prevent those infected from holding any position that would bring them about the posts at night. The routine examination of the blood of recruits for the Scout organizations would keep many men so affected out of the service, thereby removing a source of infection to their fellows. While filariasis of itself is apparently in no way incompatible with the enjoyment of excellent health, the possibilities of its sequelæ should not be lost sight of. The discovery and rejection of these men before enlistment would be the most satisfactory method of prevention.

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[5] *This Journal* (1908), 3, 311.

VIII. SUMMARY AND CONCLUSION.

It is evident that filariasis is not as rare a disease in the Philippine Islands as has been supposed. From our own observations and the fact that seven out of nine previously reported cases of filariasis among the native population have been natives of the Bicol provinces, we are convinced that in these districts we have the largest endemic focus of filarial disease, with, perhaps, the exception of Davao, that exists in these Islands. It is our belief that the microfilaria found in the cases here reported are the *Microfilaria bancrofti,* more commonly known as the *Filaria nocturna,* and that this is the common filaria of the Islands. It is also our belief that all microfilaria heretofore coming under our observation have been examples of this same species.

In conclusion we wish to express our appreciation of the assistance given us by the governor of Albay Province, to the various municipal physicians of the Bicol provinces in general, and to Captain C. C. Collins, Medical Corps, United States Army, medical officer at Camp Daraga, who, by his zeal and energy, assisted us greatly in collecting the material for this investigation.

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ILLUSTRATIONS.

PLATE I.

FIG. 1. Elephantiasis of right leg and left forearm. Tuberose growths upon dorsum of foot.
2. Elephantiasis of both legs and scrotum.
3. Elephantiasis of both legs in a boy of 12 years.

PLATE II.

FIG. 1. Elephantiasis of right leg and scrotum, and varicose groin glands. Filarial embryos were found in the man's blood and in the fluid obtained by tapping the scrotum.
2. Elephantiasis of right leg and thigh.
3. Elephantiasis of left leg. Filarial embryos in blood.

PLATE III.

FIG. 1. Elephantiasis of foot and leg, showing warty growth over foot and ankle.
2. Elephantiasis of left leg.
3. Elephantiasis of both legs and scrotum.

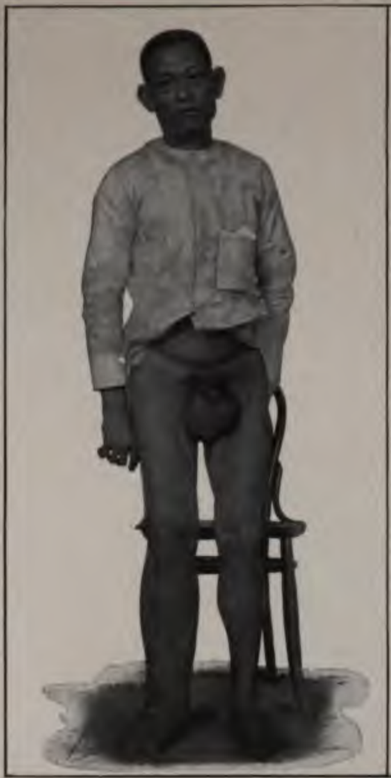

FIG. 1.

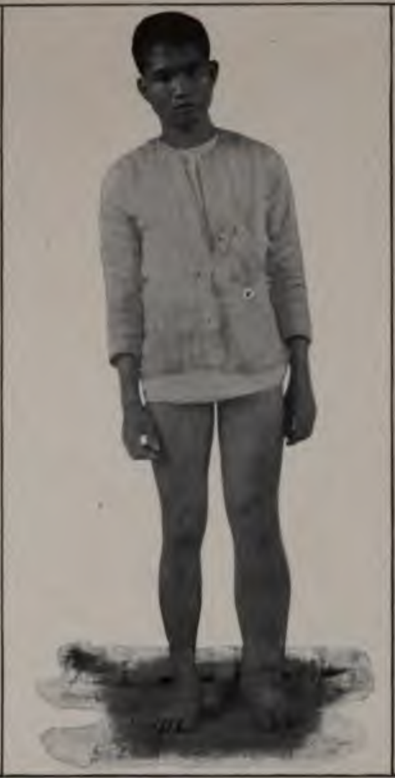

FIG. 2.

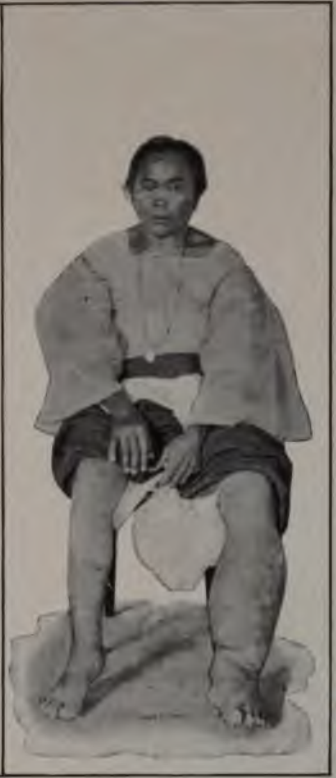

FIG 3.

PLATE II.

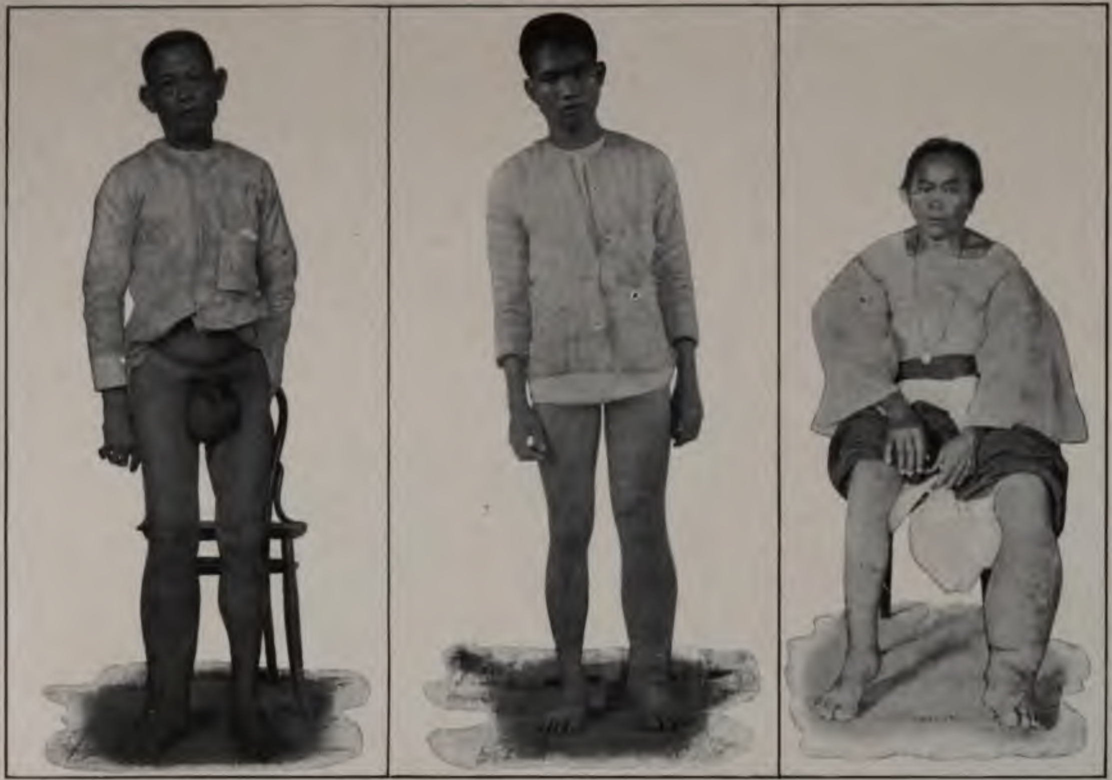

FIG. 1. FIG. 2. FIG 3.

PLATE II.

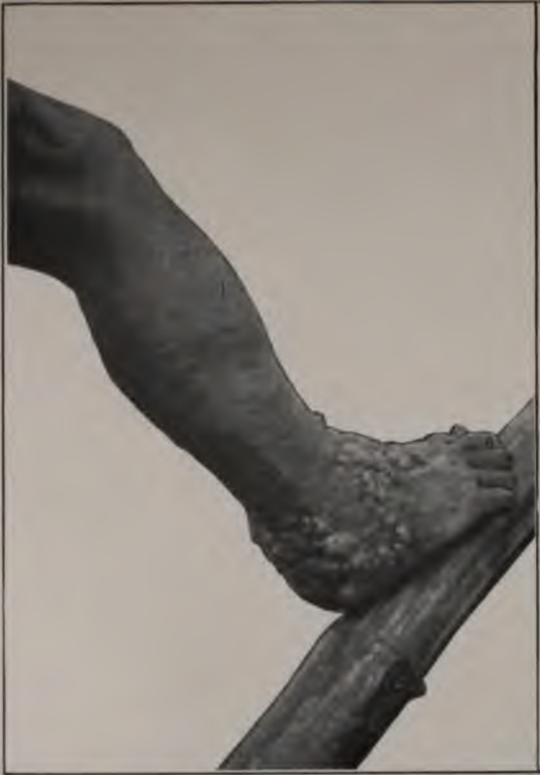

FIG. 1.

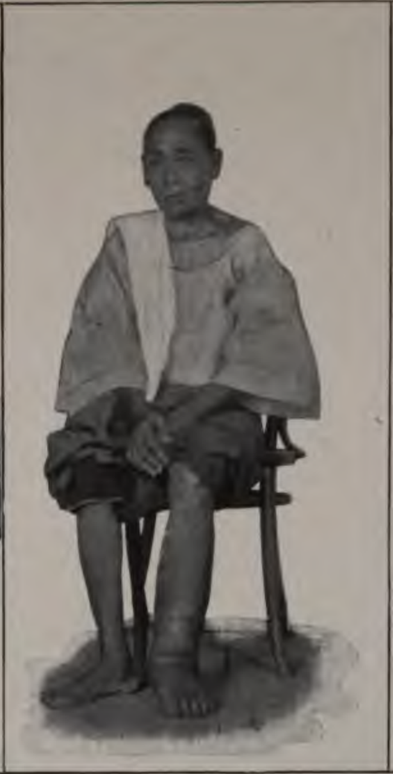

FIG. 2.

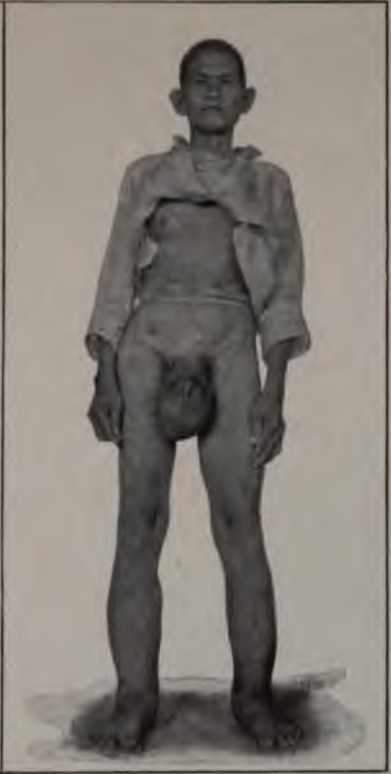

FIG. 3.

PLATE III.

NOTES ON THE DISTRIBUTION OF FILARIA NOCTURNA IN THE PHILIPPINE ISLANDS.

By **James M. Phalen** and **Henry J. Nichols**.[1]

The origin of filariasis in the Philippine Islands, as well as that of most other diseases is, and apparently must remain, a matter of conjecture. Anthropologists are not agreed as to whether the Philippines in their island form ever had any original inhabitants or, if so, who they were. However, Foreman states that, at the present time, "the Filipinos are a mixed people, descendants of Papuan, Arabian, Hindoo, Malay, Japanese, Chinese, and European forefathers." *Filaria nocturna* is common in China, India, Samoa, the Friendly and Society Islands, but we have no data to decide from which of these places, if any, the parasite was originally introduced.

Our data on the present distribution of filariasis relate only to *Filaria nocturna*, as this is the only one we ourselves have observed. As we have shown in the preceding paper, southeastern Luzon is a marked focus of filariasis, over 10 per cent of 80 persons from Albay Province being infected. Unpublished reports lead us to believe that the same may be true of Davao, Mindanao, and possibly of the east coast of Samar. Outside of these regions we have the results of the examination of 1,178 of the general population, which are as follows:

Place.	Number examined.	Number infected.	Per cent infected.	Filipinos.	Moros.	Japanese.	Chinese.
Parang	267	6	2.3	114	95	39	19
Cotabato	188	3	1.5	159	29		
Cudarangan	115	6	5.2	115			
Duluan	60	0	0		60		
Overton	113	1	.8	113			
Cebu	203	2	.9	202			1
Manila	232	11	4.8	230			2
Total examined	1,178			933	184	39	22
Total infected		29		25	3	1	0
Total infected (per cent)		2.5		2.6	1.6	2.5	0

Of 74 women, 3.4 per cent were infected.

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[1] James M. Phalen, captain, Medical Corps, United States Army, and Henry J. Nichols, first lieutenant, Medical Corps, United States Army, constituting the United States Army Board for the Study of Tropical Diseases as they occur in the Philippine Islands.

SUMMARY OF CASES.

Parang.—Of 267 residents of Parang, Bacolod, and the quarters near the dock, 6 cases—3 Filipinos, 2 Moros, 1 Japanese—were found infected. Two of the Filipinos were young muchachos who had been employed in officers' families in near-by posts for several years. One, 19 years of age, was born in Misamis and the other, 16 years old, in Cotabato; both had traveled about the island a good deal. The third Filipino, found by Captain Rand, M. C., was employed in one of the infantry companies. He was born in Misamis and had also traveled about the island. The two Moros, 19 and 30 years of age, were quartermaster employees; they were born near Cotabato; all of their life was spent in this section of the country. The Japanese, aged 26 years, had resided in the Philippines for five years, in Luzon for three years and in Parang for two years.

Cotabato.—Of 85 men, Eighth Company, Macabebe Scouts, who had been in Cotabato valley two years, none were found infected. Of 73 men, Forty-second Company, Philippine Scouts, Visayans, 2 infected cases were found by Lieutenant Love, M. C.; both had enlisted several years ago. Among 30 Moro prisoners, one individual, 31 years of age, who had lived near Cotabato all of his life was found infected.

Cudarangan.—Of 92 men in the Forty-fifth Company, Philippine Scouts, Visayans, 4 cases, aged 22, 23, 25, and 26 years, were encountered. All of these were recruits from Ivisan, Panay, Initao and Mambogao, Mindanao, and Cebu. Of 23 women, families of members of the same company; 2 infected cases, aged 17 and 32 years were met with. Both of these had come from Davao a few months before.

Duluan.—Among 60 of Datto Piang's Moros, no cases of infection were encountered.

Overton.—Of 104 quartermaster employees; one individual 19 years old was found infected. He had been in Tacloban for thirteen years, in Manila for one year, and in Overton for five. 9 applicants for Scout service were not infected.

Cebu.—Among 203 prisoners, policemen, and Constabulary, 2 cases were found; 1 a policeman, 26 years of age, a native of Samboan, Cebu, all of whose life had been spent in different parts of the island; the other a woman, aged 26 years, the wife of a man affected with lymph scrotum. Both had lived all their lives near Limao, 6 miles from Cebu.

Manila.—Among 60 employees of the Germinal Factory, Manila; one case aged 16 years was found. He was born in Paco and had always lived there; three other members of the family were not infected. Of 169 prisoners from Manila at Bilibid Prison, 10 cases were encountered; all had been in the prison only a few months. Their ages were from 18 to 36; 4 were born and had lived in Manila; 4 had lived in Manila most of their lives; the other 2 had lived for seven and for two years respectively in Manila. Two were born in Pampanga, 2 in Bulacan, 1 in Negros and 1 in Panay. Two live in Binondo, 3 in Tondo, 2 in Santa Cruz, 1 in Santa Mesa, 1 in Sampaloc and 1 in Intramuros.

These statistics show that a small amount of filariasis is very widely distributed in the Islands. Infections can probably be found almost everywhere, if a thorough and persistent search is made. The most striking feature is the relatively large number of infections in Manila, and the small number among Moros. Datto Piang's men at Duluan are the type of the real natives of the Cotabato Valley and among them no cases of infection were encountered, while at Cudarangan, just across the river, 6 imported cases among the Visayans were found.

None of these cases showed symptoms which could definitely be attributed to filaria, but as noted above, the husband of one of the infected women had a lymph-scrotum and varicose groin glands. (Plate I.) This man, age 27, had noticed a gradual enlargement of his scrotum for nine years. His three healthy appearing children were not infected with parasites.

Periodicity was determined by the examination of specimens taken every two hours for at least one case in each place. The parasite in all showed a marked nocturnal periodicity except in one case at Parang, in which very few filaria could be found at any time either during the day or night. The morphology of the parasite in this case agreed with that observed in all the others.

We wish especially to thank Lieutenants Wiegenstein and Bugbee of Parang; Lieutenant Glass and Dr. Delacroix, of Cudarangan, and Major Dutcher, of Cebu, for assistance in these examinations. A great deal of perseverance and diplomacy was necessary on the part of the officers at Cudarangan, to induce Datto Piang to permit his Mohammedans to be examined; it was necessary to collect the blood from the forearm and not from the ear or finger.

ILLUSTRATION.

PLATE 1. Lymph-scrotum and varicose groin glands. 309

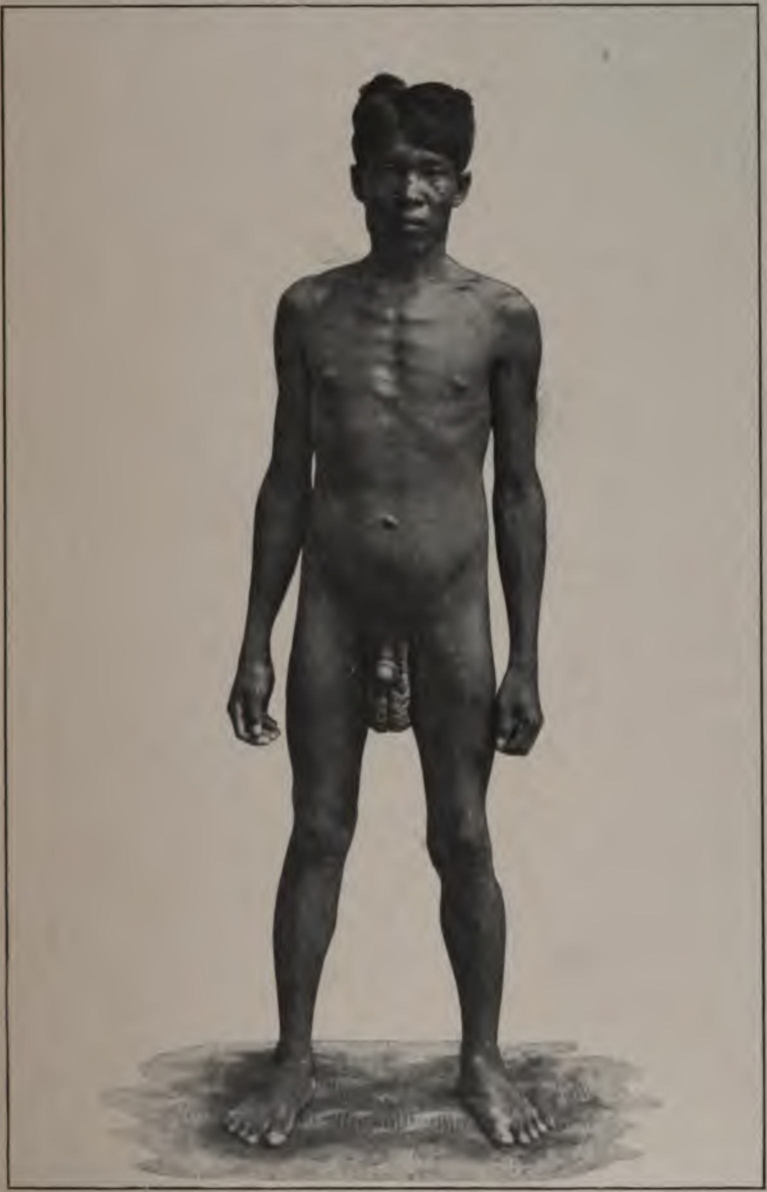


PLATE I.

OBSERVATIONS ON A PALLIATIVE TREATMENT OF ELEPHANTIASIS.[1]

By ALDO CASTELLANI.[2]

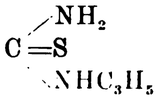
Elephantiasis is considered to be an incurable infection except in those cases where the scrotum is affected or where there are localized, pendulous tumors which may be treated surgically. For some time past I have been experimenting with a view to devising a palliative treatment for this disease, which is extremely common in some parts of the tropics. At first, following the example of my predecessors, I tried injections of various antiseptics with the idea of destroying the organism which causes the disease.

The chemicals experimented with were the following:

1. Methylene blue, given by the mouth as well as by subcutaneous injections.
2. Solutions of bichloride of mercury, carbolic acid, cyllin, and other antiseptics given hypodermically.
3. Various arsenical compounds: cacodylate of sodium, of quinine, etc., given by the mouth and by subcutaneous injections.

The result of the investigations was negative and not the slightest improvement was ever noticed in any case. It then occurred to me that since one of the anatomical features of elephantiasis is the enormous increase of the fibrous tissue, thiosinamin might be useful in the treatment of the disease, especially in case of long standing. It is well known that thiosinamin, according to Hebra, Van Hoorn, Lengemann, etc., has the power of softening various kinds of fibrous tissue, facilitating its absorption, although the mechanism of this action is not known.

Thiosinamin was discovered in 1828 by Berzelius; it is obtained by treating two parts of mustard essence with one part of absolute alcohol and seven parts of ammonia, heating at 40° for several hours, and then slowly cooling. The chemical formula of thiosinamin is,



$$C\overset{\diagup NH_2}{\underset{\diagdown NHC_3H_5}{=S}}$$

The crystals of thiosinamin have a bitter taste, a garlic-like odor and are easily soluble in alcohol and ether, but not in water. Thiosinamin, in addition to its peculiar softening action on various fibrous tissue, possesses also some antiseptic properties. Thiosinamin injections are very painful and I have therefore used fibrolysin, which is a water soluble combination of thiosinamin with sodium salicylate, prepared by Mendel and manufactured by Merck. Fibrolysin can be obtained in sterile glass ampullæ, each containing 2 cubic centimeters of liquid corresponding to 0.2 gram of thiosinamin.

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[1] Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, February 29, 1908.

[2] Director of the clinic for tropical diseases, Colombo, Ceylon.

I may state at once that the simple injection of thiosinamin without rest, massage, and most important of all, proper systematic pressure is not conducive to improvement.

TECHNIQUE OF THE TREATMENT.

The patient is first kept at complete rest in bed for a week, the affected parts bandaged with flannel or India rubber, and massaged regularly twice daily; they do not show much improvement as regards size after these manipulations, but they become somewhat softer. Next I begin injecting thiosinamin. I make the injections in various parts of the affected regions, using ordinary antiseptic precautions. I use an antitoxin syringe supplied with a strong needle. A sterile pad of gauze is applied at the place of the injection and the whole limb is tightly bandaged with flannel. To increase the pressure, pads of inelastic material, like stiff compressed gauze or boiled cotton wool or wood or iron bars, may be applied on the more prominent or harder parts, before bandaging. In some cases an elastic rubber bandage is applied for one hour two or three times daily over the flannel bandages directly over the skin.

The injections are almost painless; after two or three hours there may be a little pain locally, and the following day the part may feel harder than before, but in the successful cases, after two or three days the spot where the injection was made and the parts surrounding it become softer. As regards dosage, I generally inoculate 2 or 3 cubic centimeters of fibrolysin every day or every other day, according to the features of the case, for about a month, and then discontinue the injections for a week, during which time the use of flannel and India-rubber bandages is continued. The India-rubber bandaging is most useful in cases of elephantiasis verrucosa, because it has no action on the deep lesions of the disease, but renders the skin much smoother, the hard verrucose-like projections disappearing or becoming smaller. The disappearance of the hard, corneous formations is facilitated by applying before bandaging a spirit lotion containing resorcin and salicylic acid, 10 grams of each to thirty of rectified spirit. After a week or ten days, a second course of thirty or more injections is given; then again a week's rest with rubber bandaging, followed by another course or several other courses of injections. It is to be noted that while rubber bandages are very useful in elephantiasis verrucosa, they are of very little advantage and occasionally may do harm in those cases of elephantiasis which present a smooth skin.

After this treatment, the affected parts, in successful cases, are of much smaller size, although the enlargement of the bones so frequently found does not decrease. The skin becomes softer, more elastic, and can be pinched up in folds.

At this stage, when most of the subcutaneous tissue has been absorbed, I suggest the surgical removal of the portions of the redundant skin, when the disease affects the legs. Long elliptical strips of skin and the subcutaneous tissue are removed and the margins of each wound stitched together. This would not be practicable before the medical treatment, as the coaptation of the opposed surfaces of the skin, they being enormously thickened and elastic, would not be feasible. When the wounds have healed, the patient is advised to wear elastic stockings and every night for an hour, an elastic bandage.

CASES TREATED.

CASE. 1. *Elephantiasis verrucosa of the right leg.*—Ganegada Singhappu, Singhalese, 18 years old, admitted to the clinic January 2, 1907. The first symptoms of the disease appeared twelve years ago, when he suffered from repeated attacks of fever accompanied by painful temporary swelling of the right leg. Later on the enlargement of the leg became permanent, increasing gradually to such an extent that the patient had to give up his work. He was an indoor servant.

At the time of admission the whole limb below the knee was greatly enlarged, the skin being thickened, hard, and rough; on the dorsum of the foot and toes, numerous, horny, hard prominences were present. The limb measured round the ankle, 23½ inches; round the calf, 25½ inches; the inguinal glands were not enlarged, the scrotum and the left leg were not affected. No filariæ were found in the blood.

The patient was first kept in bed for two weeks with the right leg slightly elevated and tightly bandaged with flannel. Massage was given twice daily. At the end of the two weeks the parts were slightly softer, but the dimensions of the leg were practically the same. The thiosinamin treatment was then begun using the precautions already mentioned.

The patient received altogether sixty-two injections. During the last period of treatment the limb was very tightly bandaged for one hour, three times daily with a rubber bandage. At the end of the course of the injections, the condition of the affected leg was strikingly improved, the circumference of the ankle being reduced to 9½ inches, and of the calf to 12 inches. Moreover, the skin had become soft and of almost normal elasticity.

The patient, finding himself so much improved and able to walk easily, whereas when admitted he could scarcely move without help, asked to be allowed to leave the clinic temporarily to go to his village where he had some business to transact. I told him to use a flannel bandage continuously, and to come to the clinic at the earliest practicable date. He returned two weeks later, confessing that he had never used the bandages given him. The lower parts of the leg and the foot were much enlarged (circumference of the ankle 12 inches), œdematous and soft. After twenty-four hours of complete rest in bed and rubber bandaging, the swelling disappeared, and the measurements of the limb gave the same results as when he had left.

The patient remained in the clinic for several weeks more without having any more thiosinamin injections. The use of a rubber bandage was, however, regularly continued; the size of the leg increased very slightly. In July I advised him that long elliptical strips of the redundant skin should be removed.

I asked Dr. Paul, surgeon to the General Hospital, to perform the operation and he very kindly consented to do so. The operation took place on the 10th of July. The patient was given chloroform and, after a thorough disinfection, a long elliptical strip of the skin and subcutaneous tissue was removed from the anterior part of the leg and dorsum of the foot. The margins of the wound were brought into contact by means of an interrupted suture. The stitches were removed after eleven days. The wound healed rapidly. Three weeks later another strip of skin was similarly removed from the posterior region of the leg. This wound also healed quickly. The patient left the hospital in the latter part of August, but has been seen by me regularly. So far, five months after the first operation, the leg is not enlarged; he has been regularly wearing an elastic stocking and at night has used a rubber bandage for an hour after having massage applied. If he does not wear the elastic stocking, and does not employ the bandage, the lower part of the leg becomes somewhat swollen and œdematous, although much less by far than before the operation.

CASE. 2.—The patient, a private case, consulted me in October, 1906. He was suffering from elephantiasis of the right thigh, leg and foot, of twenty years' duration. The skin of the lower part of the leg and foot was extremely hard, inelastic, and covered with numerous small, wart-like protuberances.

Measurements: Round the ankle, 24½ inches; round the calf, 27 inches; round the thigh, 25 inches.

The patient underwent a treatment of ninety thiosinamin injections, combined with complete rest in bed, the use of the flannel bandages at first, and the India-rubber bandages later. The case improved greatly, the skin becoming softer, more elastic, and much smoother. The circumference round the thigh was reduced to 21 inches, round the calf to 16 inches, and round the ankle to 14½ inches. The patient was able to walk with much greater ease and following my instructions, has been wearing puttees and has continued regularly the use of the rubber bandaging twice daily for an hour. He states that if he stops the bandaging and the wearing of puttees, even for two or three days, the leg becomes swollen and œdematous; the swelling disappears, however, after a few hours, rest and bandaging. He refused operation and has not been seen by me lately.

CASE 3.—The patient, a private case from India, had elephantiasis for fifteen years, confined to the lower part of the left leg and foot. He underwent a course of fifty-six thiosinamin injections, combined with rest, massage, and the use of the rubber bandages. The improvement was very slight; the skin became somewhat smoother, but the dimensions of the affected parts remained practically the same. I think that rest, massage, and bandaging alone, without the injections, would have induced the same improvement.

CASE 4.—Singhalese woman, aged 56; admitted to the clinic April 2, 1907. The disease was of fifteen years' standing, and was localized in the lower two thirds of the left leg and in the foot. The skin was thick and inelastic, but not so rough as in the other cases. Circumference round the ankle, 19 inches.

The woman was kept in bed for ten days, and the parts bandaged with flannel bandages; after this treatment the skin became softer, but the dimensions of the limb remained practically unchanged. I then began giving thiosinamin injections. After having received thirty-five injections, she left the clinic at her own request, wishing to visit her family in a distant village. She was better at the time of leaving, the dimensions of the foot and leg having greatly decreased. When the patient was admitted to the clinic she could not move her toes; on leaving, such movements could easily be made.

Case 5.—Bennet Gregory, Singhalese boy, aged 10 years; admitted to the clinic on June 25, 1907. Three years ago the patient began suffering from attacks of fever with contemporary swelling of the left leg and of the lymphatic inguinal glands of the left side. On admission, the left leg and foot were greatly enlarged, the skin being thick and hard, but with a smooth surface. The lymphatic inguinal glands of the left side were slightly enlarged and hard. The maximum circumference of the calf was 14½ inches.

Treatment was begun on June 28, 1907. He received twenty-five injections and the limb was regularly tightly bandaged with flannel and for one hour every other day with rubber bandages. On July 23 the injections were discontinued; they were resumed on the 29th of the same month. During the interval only massage and the use of India-rubber and flannel bandages were continued. After the first twelve injections a distinct improvement was noticeable, the parts having become softer and the size of the limb decreased. On July 15 and 16, however, the affected parts again became enlarged and very hard, although there was no fever. This condition lasted for three days, when on the 17th the improvement again began and steadily continued.

At the time of writing (January, 1908) the improvement is well marked, the maximum circumference of the calf being 7 inches. The skin is much more elastic and can be pinched up in folds almost everywhere. I hope it will soon be possible to perform the same operation as in *Case 1*. It is to be noted that the patient remained without any treatment during November and December, 1907, as his parents took him back to their bungalow.

Case 6.—*Elephantiasis verrucosa of the right leg.* Vekanda, Singhalese man 40 years of age. Admitted to the clinic on September 3, 1907. The disease was of fifteen years' standing; the right leg and foot were enormously enlarged, the maximum circumference of the calf being 28½ inches; the skin was thick, inelastic, and covered with numerous, hard, corneous projections; the lymphatic glands of the right side were enlarged and hard; the scrotum was not affected. Numerous *eosinophiles* (15 per cent), but no *Filaria nocturna*, were encountered in the blood.

Treatment was started on the 9th of September, 1907; the patient up to the present time (January, 1908) has received seventy-five thiosinamin injections. He remained without treatment during the month of November. The whole limb has been regularly bandaged, flannel pads, etc., being applied. The case has much improved; the maximum circumference of the calf now being 16 inches and the skin has become much softer. I propose to continue the treatment for one month and then, if the skin has become elastic, the same operation as in *Case 1* will be performed.

CONCLUSIONS.

1. The treatment I have devised for elephantiasis, namely thiosinamin (fibrolysin) injections and methodical bandaging, followed by removal of portions of the redundant skin when most of the subcutaneous tissue has been absorbed, is of utility in a certain number of suitable cases.

2. I am not yet in position to give any definite explanation on the mode of action of the treatment, which I consider only palliative. Probably thiosinamin acts by softening the fibrous tissue so profuse in elephantiasis, and possibly, the antiseptic properties of thiosinamin, though very slight, may play a certain role. An observation which, if confirmed, may throw some light on the question, is that in the majority of my cases (five out of seven), the thiosinamin injections induced a fairly well-marked, though transient, leucocytosis; in one case (Case 1) the number of leucocytes rose from 9,000 to 17,500 per cubic millimeter.

It is to be noted that the thiosinamin treatment without a constant, well-distributed pressure on the affected parts, best obtained by the application of hard pads and by careful bandaging, does not cause any marked improvement.

Constant pressure on the affected parts by means of bandaging, etc., *without* thiosinamin injections, has practically no effect in severe chronic cases, although it may be of temporary benefit in recent ones.

ILLUSTRATIONS.

PLATE I.

FIG. 1. Elephantiasis. Case 5, before treatment.
2. The same, after five months' treatment, no operation.

PLATE II.

FIG. 1. Elephantiasis. Case 6, before treatment.
2. The same, after four months' treatment, no operation.

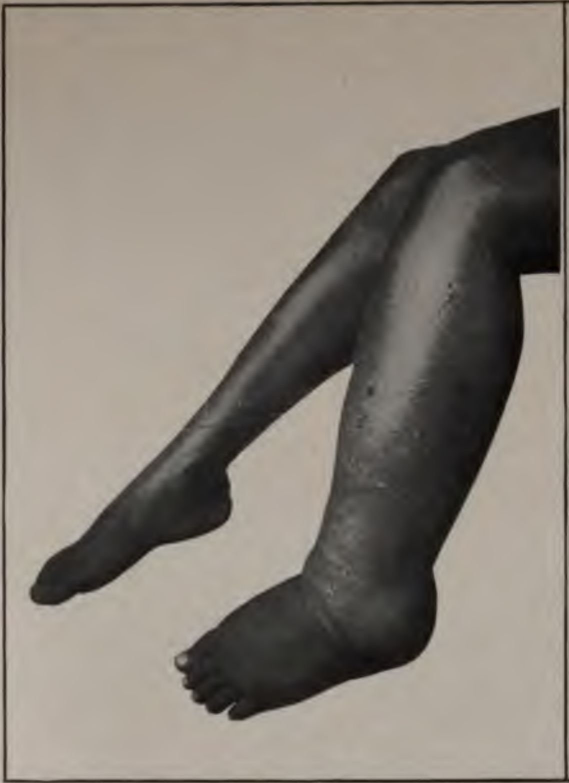

FIG. 1.

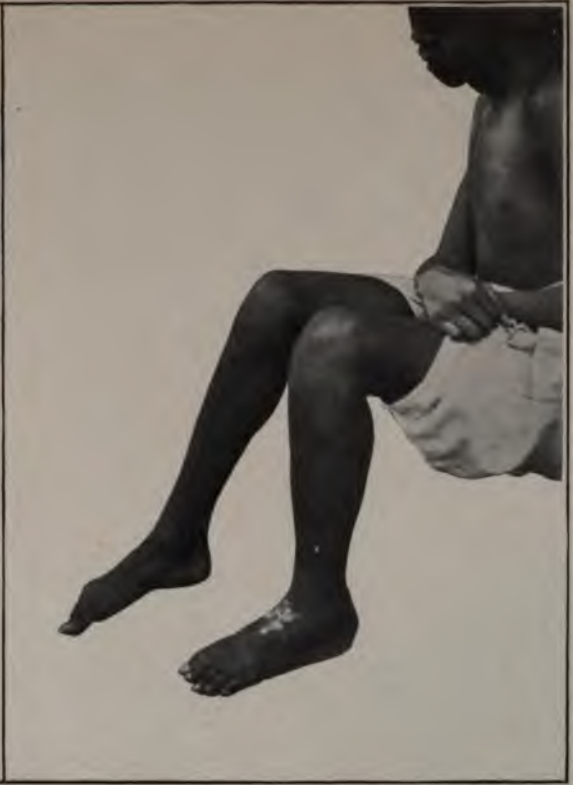

FIG. 2.

PLATE I.

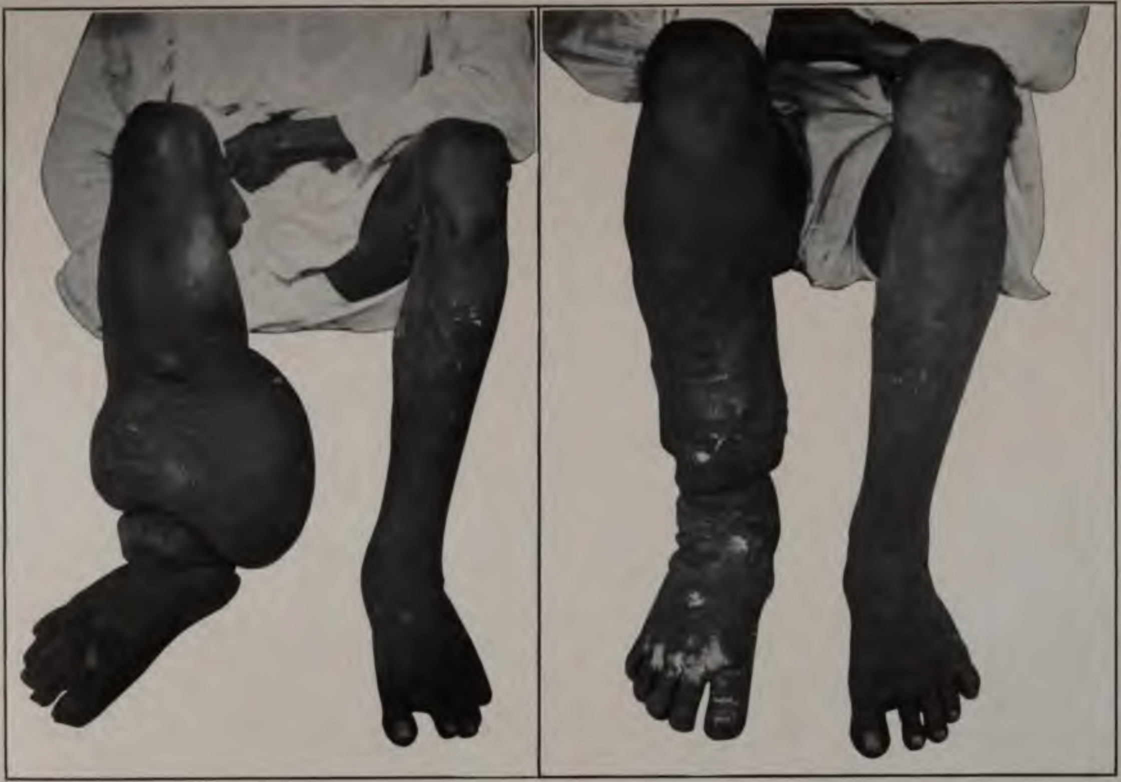

FIG. 1. FIG. 2.

PLATE II.

FURTHER FILTRATION EXPERIMENTS WITH VIRUS OF CATTLE PLAGUE.

By E. H. RUEDIGER.

(From the Serum Section of the Biological Laboratory, Bureau of Science, Manila, P. I.)

It was shown in a previous report[1] that the laked or unlaked blood and the bile of bullocks sick with cattle plague, lost the power of transmitting the disease to other animals after being passed through Berkefeld filters marked V, N or W; while peritoneal fluid retained this property on being passed through either one of these filters.[2]

It was considered necessary to repeat the experiments with peritoneal fluid with all possible precautions, owing to the danger of accidental infection of the animals used for the previous experiment. The bullocks used in the former experiments were kept in a fly-proof stable and so far as could be determined, there was no cattle plague within a radius of three miles, neither did the attendants, feed, utensils, etc., come in contact with animals suffering from that disease, nor with excreta from such animals.

The results here reported were obtained with peritoneal fluid after it had been passed through one of the following filters: Berkefeld N, Berkefeld W, Chamberland F, and Chamberland B. Five liters of citrate solution (the addition of 0.5 per cent solution of potassium or sodium citrate became necessary to prevent subsequent clotting of the fluid) was injected into the peritoneal cavity of a bullock sick with cattle plague. About one hour later the animal was bled to death, the abdomen opened and the peritoneal fluid collected.

EXPERIMENTAL.

No. 1. Peritoneal fluid obtained as above on the 13th day of January was divided into two parts, *a* and *b*. Fifty cubic centimeters of part *a*, unfiltered, were injected under the skin of bullock No. 27. The temperature of the bullock rose rapidly three days later, and on the 18th day of January, five days after inoculation, the animal was bled to death and the lesions found post-mortem were those characteristic of cattle plague. (See Chart No. 27.)

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[1] *This Journal* (1908), 3, 165.

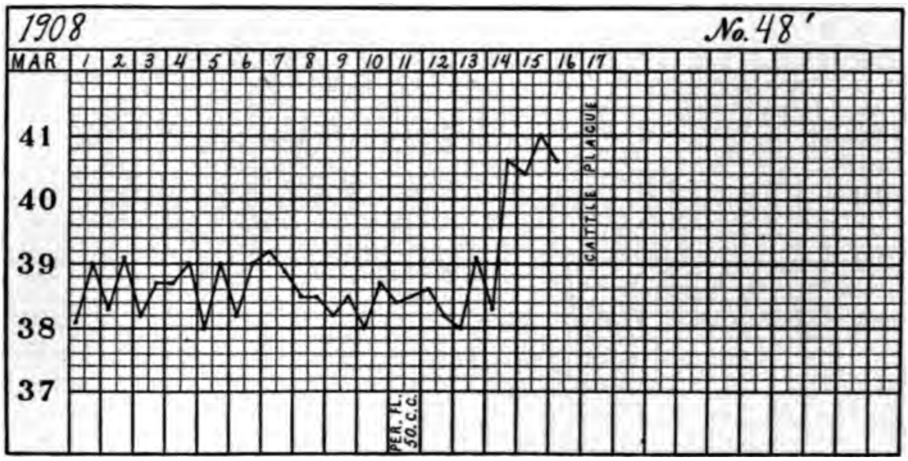
[2] The Berkefeld filters V, N, and W are coarse, medium, and fine grained, respectively. The filter marked W, the finest grained Berkefeld filter, is considerably coarser than the Chamberland filter marked F.

ILLUSTRATIONS.

Eleven charts.

ILLUSTRATIONS.

Eleven charts.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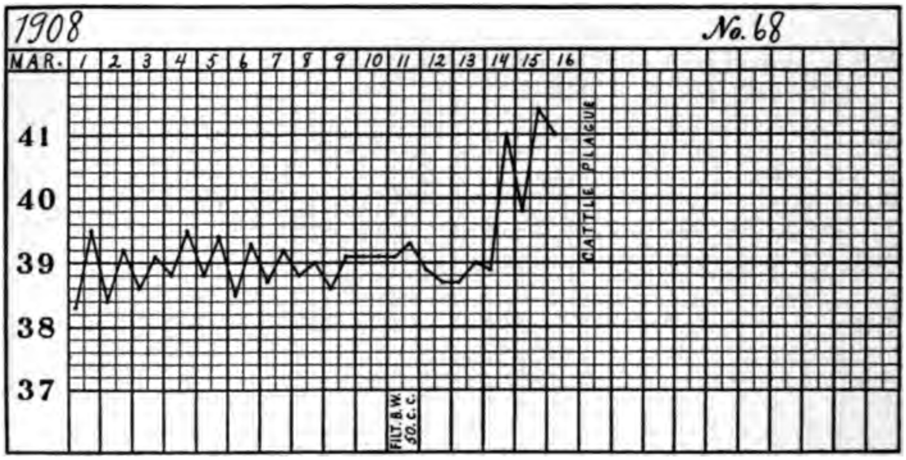
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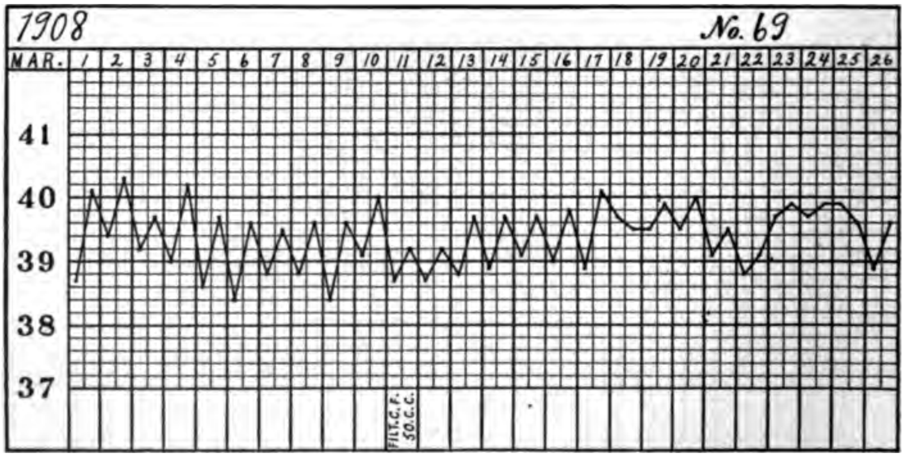
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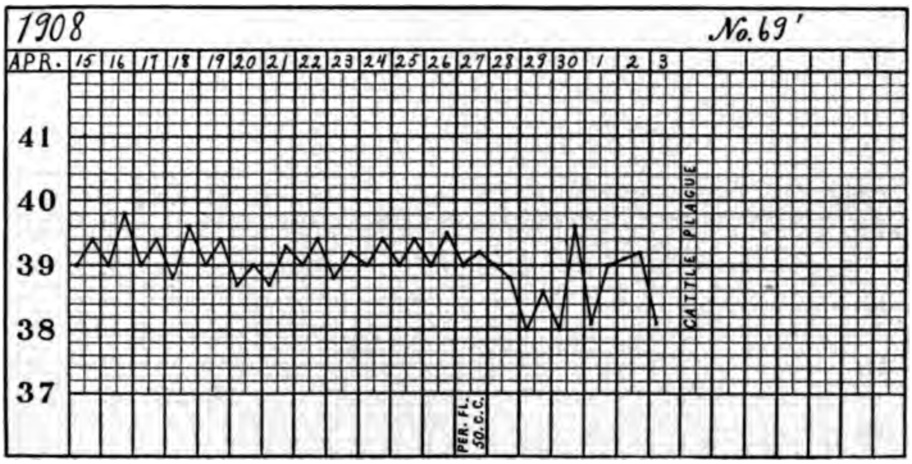
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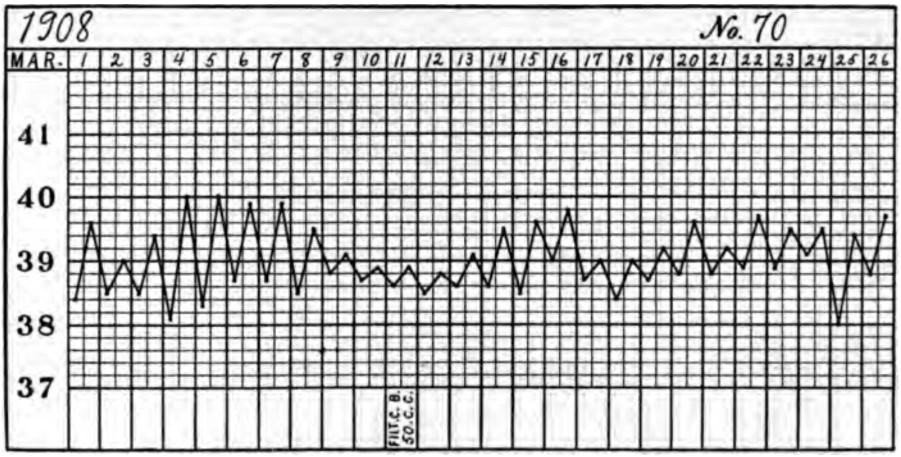
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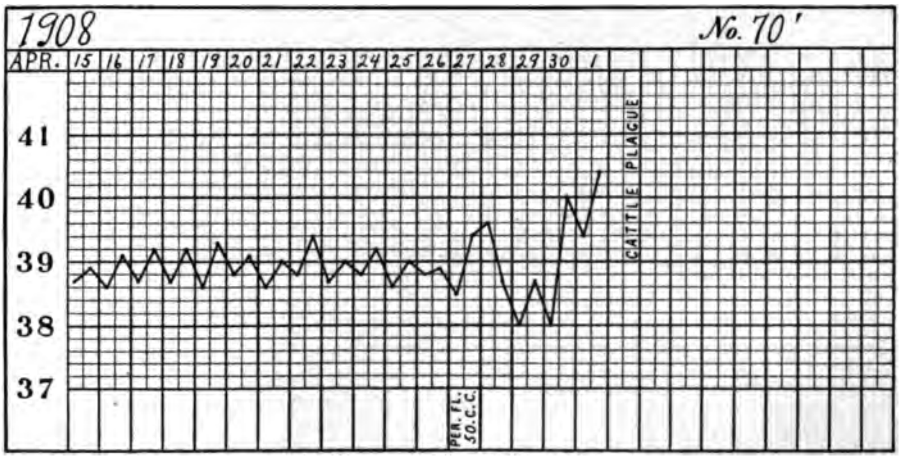
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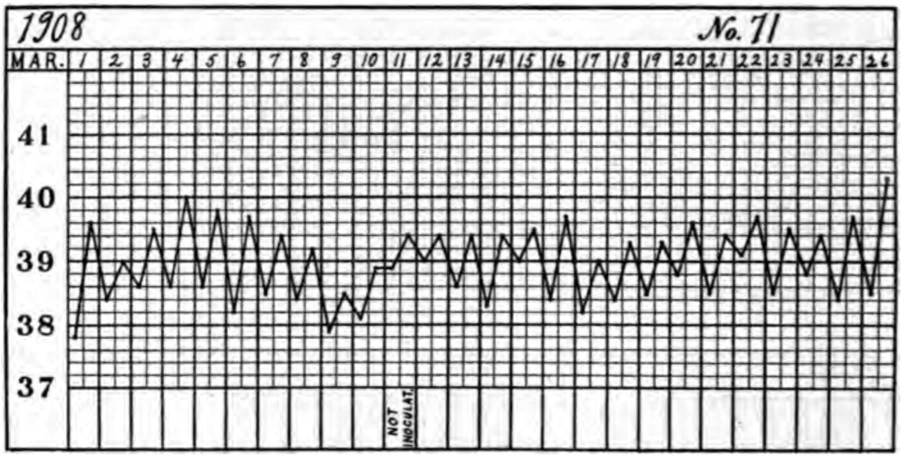
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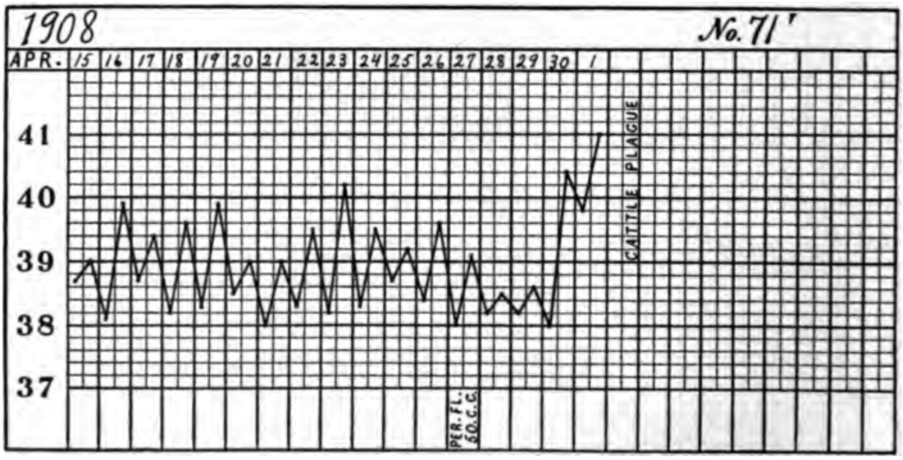
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CATTLE PLAGUE

A REPORT OF SEVERAL CASES WITH UNUSUAL SYMPTOMS CAUSED BY CONTACT WITH SOME UNKNOWN VARIETY OF JELLYFISH (SCYPHOZOA).[1]

By Edward H. H. Old.[2]

The cases reported under this title were observed during the summer months of 1906 and 1907. Two were reported from Olongapo; the others occurred in the waters of Cañacao Bay, an offshoot of Manila Bay lying between Cavite and the peninsula opposite, on which is located the United States Naval Hospital.

The first case was seen in 1906 and the account which the patient gave of his symptoms after having been stung by the jellyfish seemed so exaggerated that it was not seriously considered at the time and his actions and complaints were looked upon merely as a marked hysterical attack following an ordinary sting from one of these fish. Not until other cases were observed in 1907, were such symptoms following the sting of a jellyfish looked upon as possibly something peculiar to these waters.

Notes were made on the cases as they were observed. These notes showed a regular symptom complex, and those cases noted independently by medical officers stationed at Cavite and Olongapo go to prove that the symptoms were not accidental.

Case 1.—In August, 1906, a call was received at the hospital stating that a man, who had been in swimming off Sangley Point, had been stung by a jellyfish and was very sick.

A friend who was with him at the time said that the patient, when he came out of the water shortly after he had been stung, complained of pain over his thigh, and soon afterward of pain elsewhere; then he became prostrated and began to vomit, to cough, and to breathe rapidly. On admission to the hospital, an area of erythema slightly raised and streaked and about the size of the palm of the hand was seen on his right thigh; vomiting had ceased, but his respirations were much increased and he continued to cough almost incessantly. The cough was short and hacking in character as if a foreign body had lodged in the larynx, and a thin, mucoid sputum was expectorated. His face was congested and anxious in expression and he wept at intervals. He threw himself constantly about on the bed, seemed to be in great pain and expressed much anxiety as to his condition. As stated above, his actions were looked upon as hysterical, for this was the first case of this nature seen here.

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[1] Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, February 28, 1908.

[2] Assistant surgeon, United States Navy.

The patient was given morphine sulphate, one-fourth grain by hypodermic injection; the local condition was treated with an alkaline solution and was relieved in about half an hour. The next day he felt only a little weak, and otherwise appeared well and reported for duty.

No record of his temperature was kept; the pulse was of good force and the rate slightly increased.

CASE 2.—V., a hospital attendant at Cañacao, on June 21, 1907, while in bathing off the hospital wharf was stung by a jellyfish. He said that he was some distance from the landing and, as soon as he felt the sting, he turned back to the wharf; that on his way he felt some pain across his back, but thought it was due to swimming. On his way up from the wharf to the hospital he began to feel badly and sat down for a little while. When be reached the hospital, about thirty minutes after he had been stung, he became prostrated and had to be carried to a bed.

On arrival I found a slightly raised, vesiculated, red area over the left biceps muscle. This "wept" like an eczema. The patient was throwing himself around the bed and coughing almost incessantly, expectorating a thin mucus. He complained of nausea but did not vomit. His face was congested and anxious. He wept at intervals, a stream of tears flowing down his face. The nose was occluded as in a bad case of coryza and from it a thin mucus was discharging. He complained of pain in his head and of marked pain in the lumbar region. He expressed much anxiety as to his condition and exclaimed now and then: "I don't know why, but I've lost all my nerve." His temperature was 38° C. (100°.2 F.); pulse 100, strong and full. The examination of urine and blood showed nothing abnormal.

Morphine sulphate one-sixth grain was given by hypodermic injection, an alkaline solution was applied to the arm. The symptoms subsided shortly after and in a few hours the temperature was normal and the pulse 60. The next morning the patient felt weak and complained of a slight sore throat: the pharynx was slightly inflamed.

CASE 3.—S., a hospital attendant on duty at Cañacao on June 24, 1907, while swimming off the hospital wharf was struck by a jellyfish on the left side of his chin. He felt the sting immediately, but had no general symptoms until fifteen minutes later. Knowing the effect in the previous cases he came immediately to the hospital.

There was a small, red-streaked area and a few vesicles on the side of his chin. The symptoms began with sharp, shooting pains throughout the body, but chiefly across the posterior lumbar region. The patient felt nauseated, but did not vomit. The same symptoms of congested mucous membranes, cough with thin mucoid sputum and lachrymation, were present, but he was not hysterical. His temperature was 37°.5 C. (99°.6 F.). No treatment was given. The symptoms lasted two hours.

CASE 4.—On the same day as that on which the previous case occurred, M., a hospital attendant, was stung on the right forearm. A raised, red-streaked area appeared covered with little vesicles which "wept." He said that at first his arm felt as if paralyzed and that he could hardly use it to swim. Ten or fifteen minutes later, after reaching the hospital, general symptoms began with sharp, shooting pains throughout the whole body, but chiefly in the back. The patient felt nauseated but did not vomit. There was no cough or excessive lachrymation, nor were hysterical symptoms noticeable. An alkaline solution was applied locally. symptoms continued for about an hour.

CASE 5.—D., a hospital apprentice, while swimming off the hospital wharf was stung by a jellyfish on his arm. The symptoms appeared in about twenty minutes. I did not see him, but obtained a description of his symptoms, which were exactly like those of the other cases quoted, except that this patient did not have the severe pain in his back nor was he hysterical (this latter fact was obtained from one who saw him). The symptoms lasted two hours. No treatment was instituted.

CASE 6.—This was reported to me by Assistant Surgeon A. B. Clifford, United States Navy. The case came to the dispensary at the United States naval station, Cavite, on July 6, 1907. This patient was a Filipino seaman. He was stung by a jellyfish while in swimming. Slightly raised, red-streaked areas appeared on both arms and neck. He said this happened about an hour before he was seen, but at that time there was marked congestion of the respiratory tract with almost constant coughing and expectoration of a thin mucoid sputum. Excessive lachrymation was present. There was no vomiting or headache. Pain all over the body was complained of, but chiefly in the back. The patient threw himself about the bed in an hysterical manner. The temperature by axilla was 37° C (98°.6 F.). He was given morphine sulphate one-eighth grain by hypodermic injection and sodium bromide by the mouth. The patient became quiet shortly afterwards, but continued to have some pain over the streaked areas and in the back.

CASE 7.—Reported to me by Surgeon D. N. Carpenter, United States Navy, who had the case in charge at the United States naval station, Cavite. This case, H. D., occurred on the afternoon of August 11, 1907. While in bathing off this station the patient says that he was stung by a jellyfish. About fifteen minutes later when he reported at the dispensary the symptoms had already appeared.

Over the region of the right deltoid and scapula there was an erythematous hyperæsthetic area which was covered with perspiration and this would immediately reappear on being wiped off, or rather it "wept." The symtoms noted were: respiratory spasm, holding of the breath for several seconds with short expirations and nervous cough; venous engorgement of the jugular veins from holding the breath. The face was flushed, the skin of the face relaxed and perspiring profusely; the head felt hot; there was a discharge from the nose; the pupils were partially and equally dilated. Pain was complained of in the back and pit of the stomach. Hysterical nervous symptoms manifested themselves by great restlessness and complaint of constriction of the throat appeared. The lungs were clear. The heart was normal. The pulse regular and of good volume, about 80. The temperature was not taken.

Treatment.—The remedy advocated by the natives was first tried, namely of vinegar externally and sugar internally. This was without effect. Amyl nitrite inhalations were also given without result. Morphine sulphate one-eighth grain by hypodermic injection was administered and in five minutes the patient complained of no pain and the restlessness and hysterical symptoms had subsided.

The following cases were reported to me by Surgeon C. P. Kindleberger, United States Navy, they having come under his observation at the United States naval station, Olongapo:

CASE 8.—The patient was a Filipino boy, 14 years old, who was seen on July 16, 1907. He was stung on the right forearm by a white jellyfish; a red welt was seen over the effected area. He cried with pain, was restless and became partially unconscious. The lesion was treated locally with applications of alcohol and internally with a solution of sodium bicarbonate with bromides; he became quiet and was apparently in good condition. His father insisted on taking him home and as soon as the patient saw the water he again became hysterical. Shortly after he reached home a call was received for some one to see him, to which a hospital steward responded; he reported that the boy's heart and respiration showed signs of failure, and that he gave stimulants both by mouth and hypodermic injection, but these had no effect and the boy died at 7.30 p. m., just three and a half hours after he was stung.

CASE 9.—An American woman was stung on both forearms and hands by a jellyfish. The fingers of one hand became so swollen that a ring caused considerable constriction of the tissues. In this case there was severe pain locally; pallor from pain and fright; the pulse was weak. The patient did not sleep well for several nights because of the pain. Under lead and opium lotion the red welts and swelling began to disappear, but about three days after the sting an eruption resembling lesions of poison oak appeared on both arms and responded to treatment by fluid extract of grindelia robusta. No other symptoms were noted in this case.

The reason more cases were not seen is probably due to the fact that few if any of the men at the hospital went swimming in 1906, the one case quoted being a man from a ship anchored in the bay. In June, 1907, many of the hospital corps and few patients began to bathe every afternoon off the hospital wharf and it was then that the cases quoted appeared; a few days later the men stopped going into the water, being deterred by the sufferings of the other men.

The symptoms, as noted, appeared in from ten minutes to an hour, but usually in from ten to fifteen minutes. In the nine cases quoted, one death occurred (case 8) that of a Filipino boy. I wrote to Dr. Kindleberger about the symptoms I had observed in the other cases here, but he replied that he noticed none of them in this boy except that he was badly frightened and hysterical.

Four cases (1, 2, 6, and 7), one of whom was a Filipino, had the marked hysterical symptoms, with the incessant cough, restlessness, pain, nausea, etc., and all presented about the same picture. This is the type of case to be recognized as caused by some unknown irritant or poison.

While some of the symptoms in cases 3, 4, 5, and 9 are like those in the type named, still the marked hysterical condition was not present and the latter is what would impress a physician most on reaching the bedside.

I have been stung many times by the jellyfish found abundantly in the waters of Chesapeake Bay, Virginia, called there "stinging nettles" and "blood-suckers," but beyond the local erythema and pain no other symptoms were noticed. From this experience, and considering the sufferings of some of the above quoted cases, I can not but believe that there is some absorbable substance present in the secretion of the fish concerned. The irritation of the mucous membrane of the mouth, throat, nose, and eyes, as seen in some cases and not in others, may be explained by the fact that some of the water around the fish which contained the cell secretion came into contact with these areas; and this might also explain the nausea and vomiting, but the severe general body pain suggests the possibility of an absorbable substance, as does also the case of death in which a depressing effect was noted.

The part which such a cause might play in drowning is also of interest aside from that of diagnosis. A person when stung generally strikes out for the shore or a boat, but should he be very far away from either, and symptoms of the severe type come on while he is still beyond his depth, I doubt if he would be able to reach the land safely.

The particular variety of jellyfish that causes these symptoms so far is unknown to me. I made inquiries among the fishermen along the shore near the hospital concerning the nature of this fish, but although they disagreed as to which variety caused the sting, they agreed that there was one which made a man sick when he was stung, and mentioned vomiting as one of the symptoms after the sting. Some said it was the red variety, which is the most common in the water thereabouts through the summer months; while others said the white variety was the factor. Several attempts were made by men at the hospital to produce these symptoms artificially by rubbing the fish, both the red and the white varieties, on their arms and legs, but with no result. I do not believe that the sting comes from the common variety, but from one less frequently seen. Some of the men said they were stung by the red fish, others by the white, but none of them waited to capture their tormentor.

I used some alkaline solution locally and morphine sulphate hypodermically for the treatment of such cases. The alkaline solution was employed on the basis that the irritant was of an acid type, as formic acid has been generally looked on as the agent in the different kinds of stings, including those of ants, bees, jellyfish, etc. As the patients seemed to suffer a great deal and were so anxious about their condition, morphine sulphate was resorted to.

I hope that should any such cases be seen during this coming summer by the members of the Philippine Islands Medical Association they will be able not only to locate the culpable variety of this particular kind of fish, but also be able to determine the nature of the irritant or poison secreted.

A MOSQUITO WHICH BREEDS IN SALT AND FRESH WATER.

By Charles S. Banks.
(*From the Entomological Section, Biological Laboratory, Bureau of Science, Manila, P. I.*)

INTRODUCTION.

The finding of members of a given species of animal breeding under such different conditions as those which obtain in fresh and salt water, especially where experiments have proved that a given lot of individuals when found in salt water and transferred to fresh for purposes of observation, have invariably died before reaching maturity, becomes a matter of the gravest economic importance; more particularly so when the question narrows itself down to the discovery of a pathophoric mosquito having such habits.

It was stated by me in a former publication[1] that while the majority of mosquitoes breed in fresh water, and while few are known to breed in the water of the sea, yet *Myzomyia ludlowii* Theob. is among this number. This form of mosquito has been proved to be a transmitter of malarial fever. The statement[2] was also made that this mosquito had never been found in these Islands breeding in fresh water; that as a result of transferring a large number of larvæ from sea to fresh water, all had died; and putting them into sea water at the point of saturation likewise killed them.

The interesting and crucial feature of this discussion develops as the result of a trip to the mountain Province of Lepanto-Bontoc to investigate an epidemic of malarial fever, said by the officials in that region to be of the most pernicious type.

Naturally, I expected to meet with another species of mosquito causing malaria in this isolated and elevated region, but instead I encountered adults of *M. ludlowii* Theob. in the dwellings during the first night of my stay in Cervantes, the capital of the province, and I was greatly astonished to find *their larvæ breeding in the greatest abundance in the rivers and small streams of the vicinity*, while a thorough search extending over two weeks and including the rice fields, which were flooded at this time of the year, the water tanks near buildings, the streams, the wells, and in fact all probable breeding places revealed no other species of *Anophelinæ*.

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[1] *This Journal, Sec. B.* (1907), 2, 513.

[2] *Loc. cit.*

GEOGRAPHY AND TOPOGRAPHY.

The town of Cervantes is situated near the center of the subprovince of Lepanto. It lies at an altitude of 508.8 meters upon a north-south hill 60 to 80 meters high between, and south of two forks of the Abra River. Each of these forks flows through a rather flat valley which favors the wandering of the streams from their habitual channels so that in reality from about 1 kilometer above the town to approximately a kilometer below there are, in the bed of each fork, four or five subparallel streams running more or less obliquely to the main course of the river as shown on Map 1. The entire river bed is covered with rocks of various sizes, some of which are sufficiently large to impede or change the course of the stream during the dry season.

The hill upon which Cervantes stands is composed of primitive rock of which the principal constituent is diorite with a more or less eroded, clayey, top soil. The base of this hill is cut into small, sharp gullies by the action of the water during the rainy season and in many of these gullies during the dry period there are springs, usually with a very small and slow flow. *Algæ,* upon which the mosquito larvæ feed, accumulate upon the wet rocks in these springs.

This entire valley lying between the *Cordillera Central* and the *Cordillera Occidental* has but one outlet to the sea, namely through Abra Pass, which is north of Cervantes. The mountains to the west average 1,000 meters in height while those to the south reach an elevation of 2,200 meters.

The town of Sagada lies 17 kilometers northeast of Cervantes at an altitude of 1,445 meters, on the east side of the *Cordillera Central* and in a region of limestone formation. A number of small streams and springs are found in its vicinity and some of these are subterranean.

Bontoc, 8.5 kilometers due east of Sagada, in the subprovince of Bontoc, has an altitude of 842 meters and lies on a slightly elevated bluff on the Anguinak River (*Baduyan* or *Cagayan*).

The valley through which the Anguinak flows in the region of Bontoc is narrow south and southwest of the town, but widens east of it, allowing the river to divide into several streams during the dry season, but during the rainy period making it a wide, impassable current. There are a number of islands in the stream below the town during the dry season, several of which are shown on Map 2, and one toward the northeast. These islands have practically the same formation as the ones in the inner bed at Cervantes and facilities of the same character, but in less degree, are offered for the breeding of *Myzomyia ludlowii* Theob.

CLIMATE AND TEMPERATURE.

The inhabitants of the region about Cervantes state that the temperature at that point, in the daytime during the dry season, is little if any lower than that of Manila, and certainly this was so during my stay there; the average day temperature was 30°, the night temperature 25°, which was even higher than in Manila. At Sagada the thermometer ranges at a very much lower point, while at Bontoc it is slightly lower than at Cervantes.

Cervantes is surrounded by hills on all sides except toward the north, and so the town is cooled only to a moderate degree, even during the monsoons, by the breezes which blow from that direction. The breezes become heated by passing through the valley from the northern extremity and find no outlet at the south; hence Cervantes during the dry season is subjected, as it were, to an almost continuous sirocco-like wind, which circulates and recirculates within the bowl-like valley.

This region, like others in the Philippines, is subject to occasional showers during the dry weather, but at Cervantes these are very infrequent.

CHARACTER OF THE RIVER AND SPRING WATER.

While the water in this region is strongly impregnated with lime, one of its peculiar features appears to be its large content of aluminium sulphate, which is also a characteristic of the water found in the breeding places of *Myzomyia ludlowii* Theob. at Olongapo. Many of the springs near Cervantes are hot and the water from these and the cold ones evaporating during the dry season, leaves an incrustation which when analyzed in the laboratory yields, approximately, 33 per cent of aluminium sulphate.

OBSERVATIONS ON MOSQUITO LARVÆ.[3]

The larvæ of *M. ludlowii* Theob., found in the Province of Lepanto-Bontoc, were always observed in water in which algæ were growing, either floating on the surface or attached to the stones over which the water trickled. This same fact was noted in a previous publication referring to the same species of mosquito at Olongapo. Those observed in streams from springs were most abundant where there were slight depressions in which water a half centimeter or more in depth might collect; in the rivers they were always encountered where an obstructing rock or the friction of the bank caused either a back current or an eddy and where the water was comparatively still. It was very difficult to discover the larvæ in such situations except during periods of the brightest sunshine and then only when, after disturbing the surface, the investigator patiently awaited their reappearance at the top. Any motion on the part of the observer, or a shadow caused by any object passing near, would send the full grown larvæ to the bottom, while the smaller ones would hide themselves in the entanglement of the *algæ*. The most practical way of obtaining the larvæ was to dip up *algæ* and water in a porcelain plate whereupon each larva, however minute, was at once thrown into silhouette against the white background.

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[3] *This Journal, Sec. B.* (1907), 2, 518.

No difference, either in general or in minute appearance could be observed, even upon microscopic examination, between these larvæ and the ones which breed in salt water. The breeding places were in every case exposed to the direct rays of the sun; often no vegetation was present within 10 or 15 meters of the streams. Culicine larvæ of a species not yet determined were associated with those of ***Myzomyia*** *ludlowii* Theob. This former species has been found breeding in open fields in the city of Manila in water containing algæ, but has never been seen in salt water at places on the sea where the larvæ of *M. ludlowii* Theob. have been encountered.

The mosquito larvæ were found breeding at Sagada and Bontoc under conditions identical with those at Cervantes, so that the question of altitude with reference to the influence upon the species appears not to enter into the discussion as to why these mosquitoes should be found thriving under such different environments.

DEDUCTIONS AND CONCLUSIONS.

I am not aware of any other record of a species of mosquito propagating naturally in both salt and fresh water. Previous laboratory experiments along this line made by me, both in America and in the tropics, have always demonstrated that mosquito larvæ removed from fresh to salt water or *vice versa,* have perished within a short time, either as a direct result of the difference in media or because of the effect of either fresh or salt water upon their food. No attempt has been made by me gradually to transfer *M. ludlowii* Theob. from salt to fresh water and it was likewise impossible at the time of my visit to Cervantes to bring living larvæ from there to the coast for experiment.

There are two theories which might be advanced to account for the different environments of *M. ludlowii* Theob. One is that the insects, originally salt-water breeders, have gradually been migrating by way of the Abra and Cagayan Rivers from the mouth of the latter up toward the higher regions, adapting themselves slowly first, to the brackish waters near the sea, then to the tidal fresh waters and finally extending up as far as Sagada and Cervantes.

The other and more natural deduction, in view of the fact that most mosquitoes are fresh-water breeders, would be that originally all mosquitoes breed in fresh water. This would appear the more reasonable since very many species breed in isolated water and in forests far inland.

If this was the case with *M. ludlowii* Theob., then the ease with which the larvæ might be carried by the river currents toward to sea would explain their present marine or littoral habitat.

HYGIENIC FEATURES.

The most important feature of this discovery from an economic standpoint appears to be its bearing upon the general dispersal of pernicious malaria in the Philippines. There would appear to be no barrier against it from the standpoint of geographical position, either in altitude or in remoteness from the sea. In fact, the demonstration of the parasites of æstivo-autumnal malaria in individuals who have never been out of the highland region, would be an accusation of overwhelming force against *M. ludlowii* Theob., which has already been shown to carry the same parasite at sea level.[4]

In Cervantes the crescent form of the parasite was found in the blood of a little girl, P. C., aged 6 years and 5 months who had been suffering from chills and fever for about two months previous to the time when I saw her. She had always lived in the town of Cervantes and therefore certainly contracted the disease locally and with *M. ludlowii* Theob. as the transmitting agent.

CONCLUSIONS.

The most obvious conclusions are:

That *Myzomyia ludlowii* Theob. is a species which, in the Philippines, breeds in both salt and fresh water.

That altitude has (up to 1,500 meters) no appreciable influence upon its development.

That there is little hope of ridding a community, like Cervantes, of this insect, owing to the peculiar topographical features which are practically irremediable because of their extent.

That the present investigation made in a region where *M. ludlowii* Theob. is found in great abundance and where no other anopheline was encountered, gives a strong additional proof of its rôle as a transmitter of *æstivo-autumnal* malaria.

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[4] *This Journal, Sec. B.* (1907), **2**, 531 et seq.

ILLUSTRATIONS.

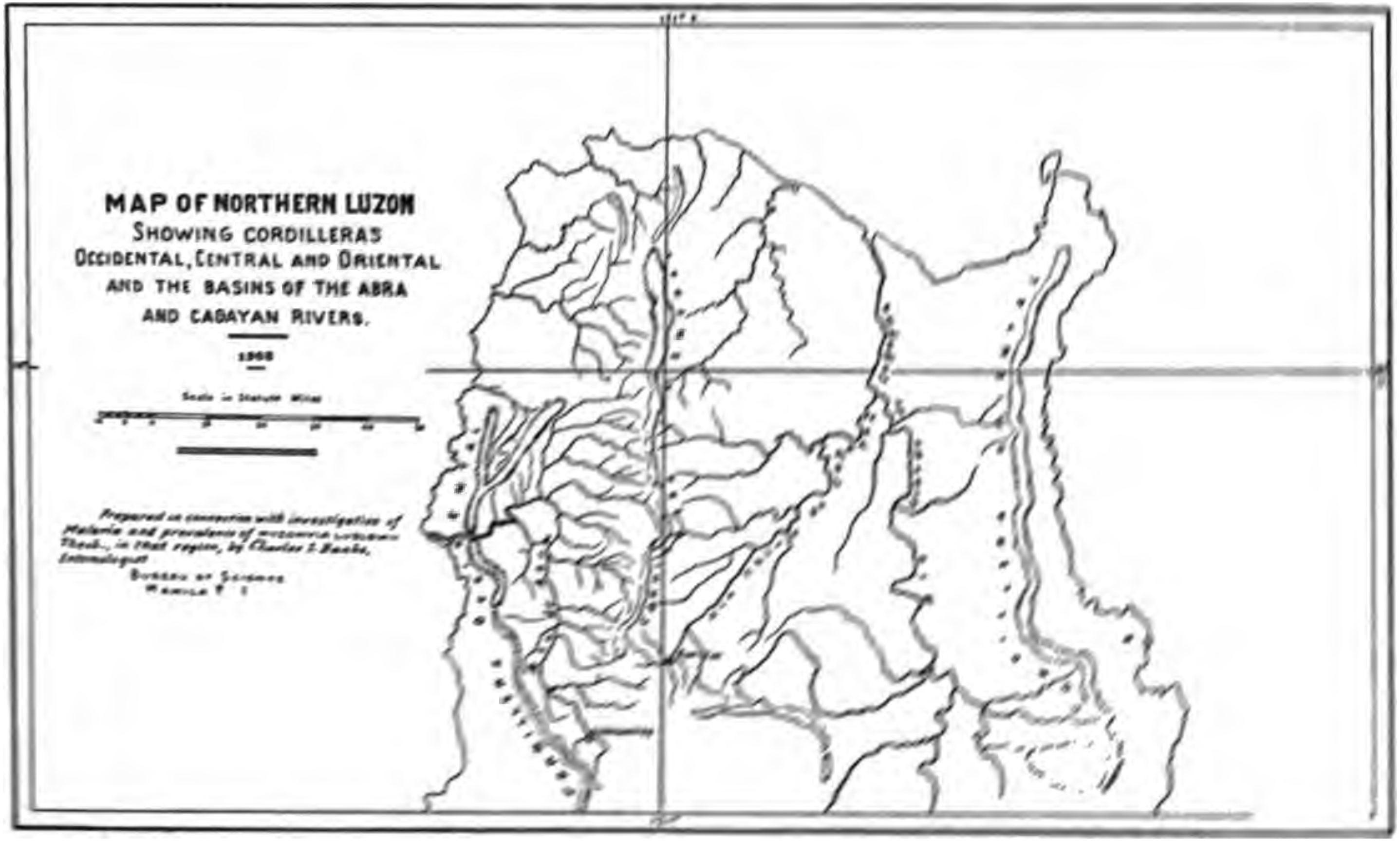
MAP 1. Sketch of northern Luzon showing *Cordilleras Occidental* and *Central* with the courses of the Abra and Cagayan Chico Rivers.

2. Town of Cervantes and vicinity showing character of Abra River bed at this place.

3. Towns of Sagada and Bontoc, showing character of Cagayan River bed near Bontoc. Note the great width of the river south and northeast of Bontoc. In the dry season the river channel breaks up into a series of small streams which make ideal breeding places for *Myzomyia ludlowii* Theob. This condition is worse at Cervantes than at Bontoc.

PLATE I. Dam in the Cagayan Chico River near Bontoc with a view of the island below it and the streams which traverse the island. Bontoc lies around behind the hill at the left.

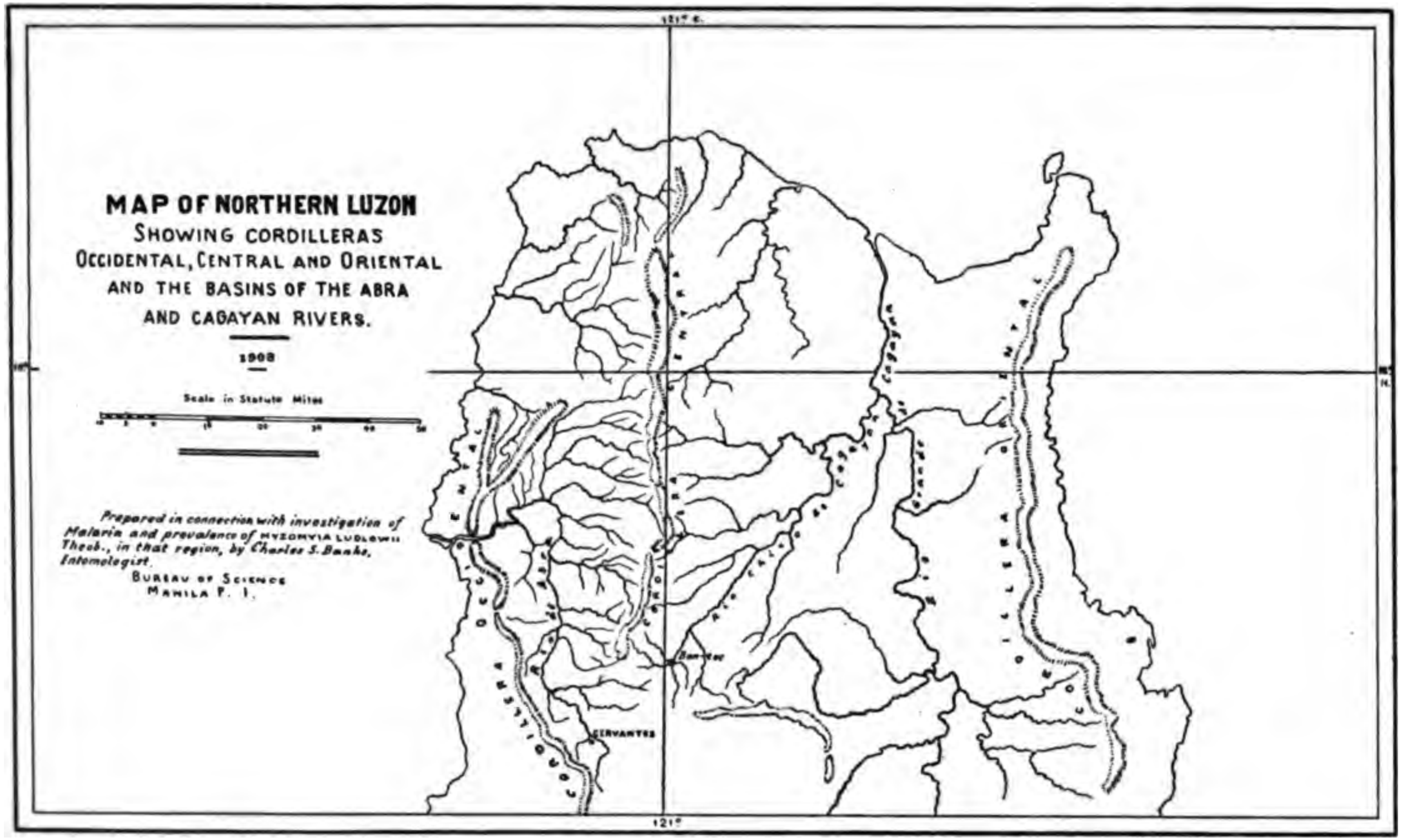
II. Cagayan Chico River, showing a characteristic spot favorable to the breeding of mosquitoes. The Abra River at Cervantes is of the same type.



MAP OF NORTHERN LUZON
SHOWING CORDILLERAS
OCCIDENTAL, CENTRAL AND ORIENTAL
AND THE BASINS OF THE ABRA
AND CAGAYAN RIVERS.

1908

Prepared in connection with investigation of Malaria and prevalence of Myzomyia ludlowii Theob., in that region, by Charles S. Banks, Entomologist
Bureau of Science
Manila P. I.



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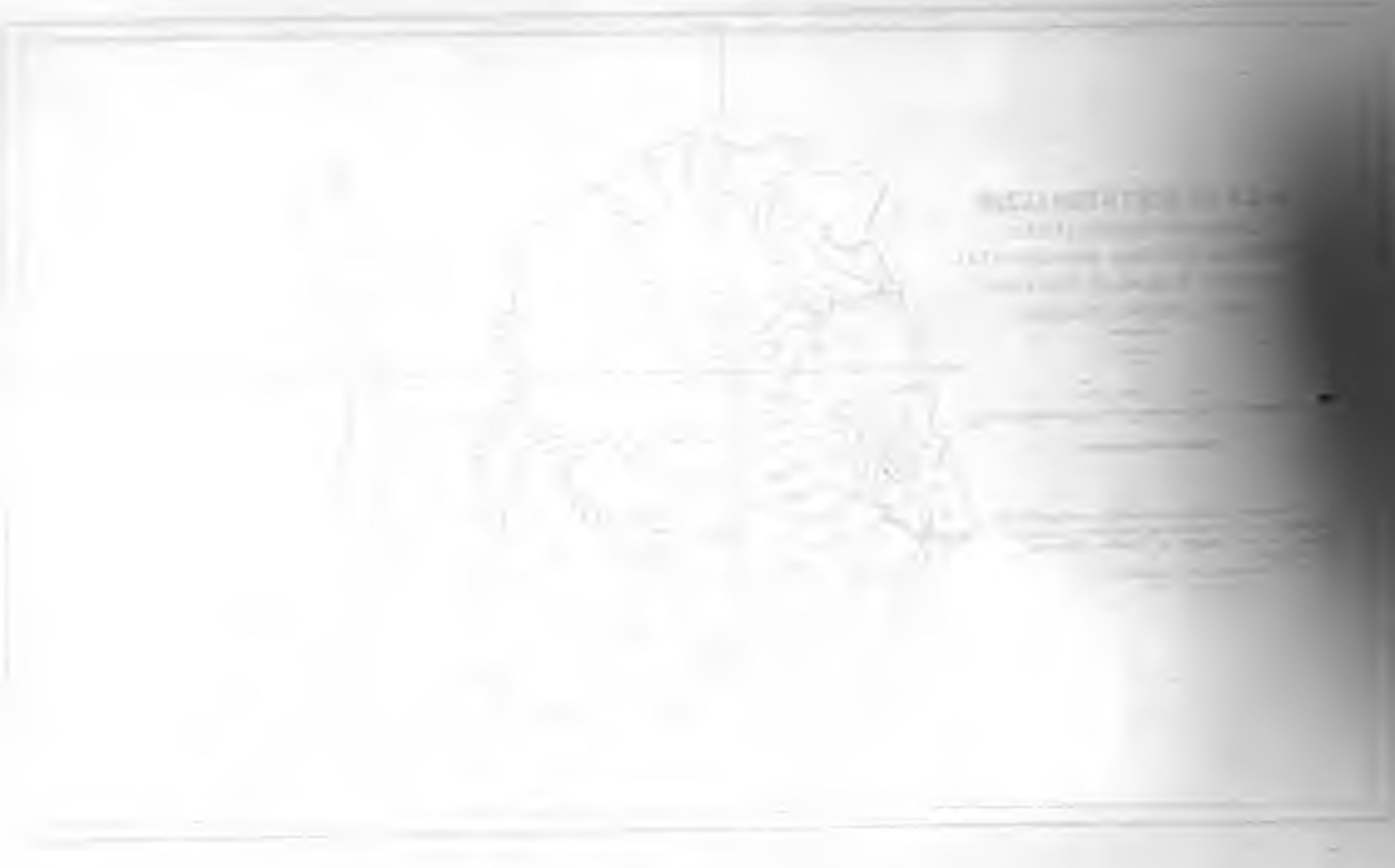
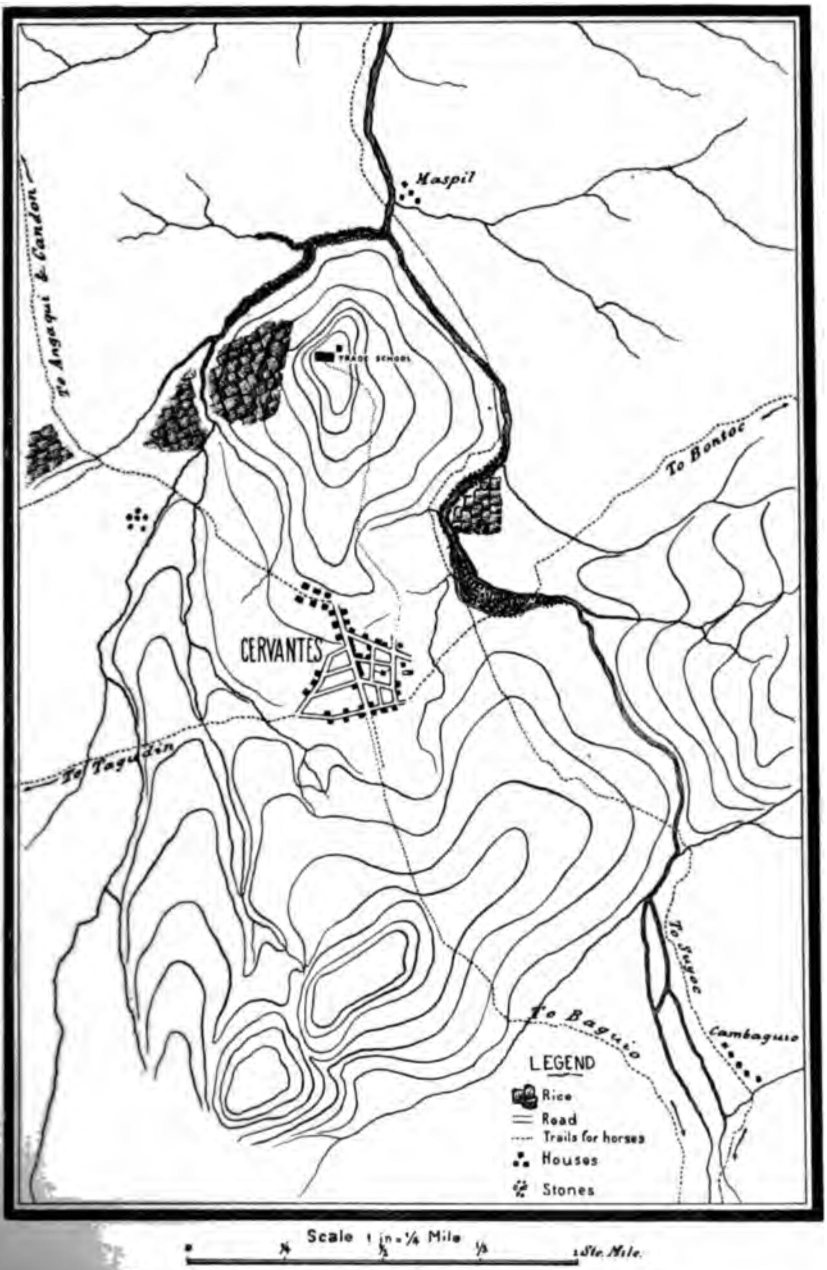
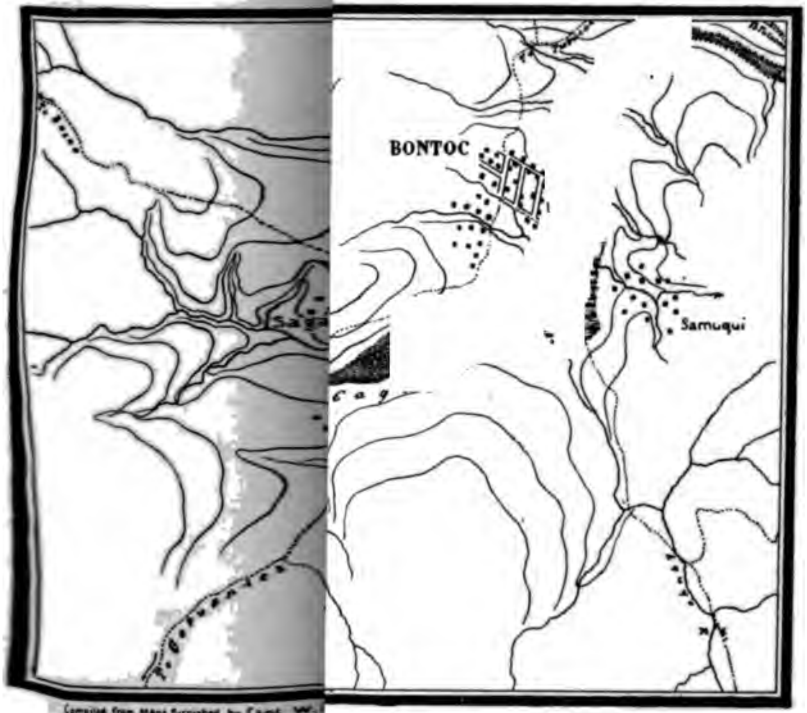
BUREAU OF SCIENCE
MANILA P. I.





MAP OF CERVANTES, PROVINCE OF LEPANTO-BONTOC.



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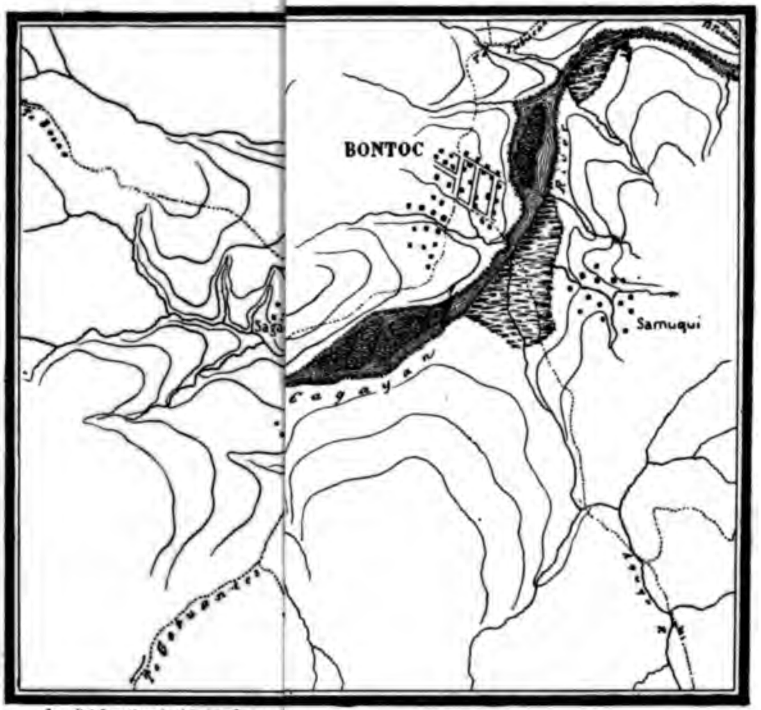

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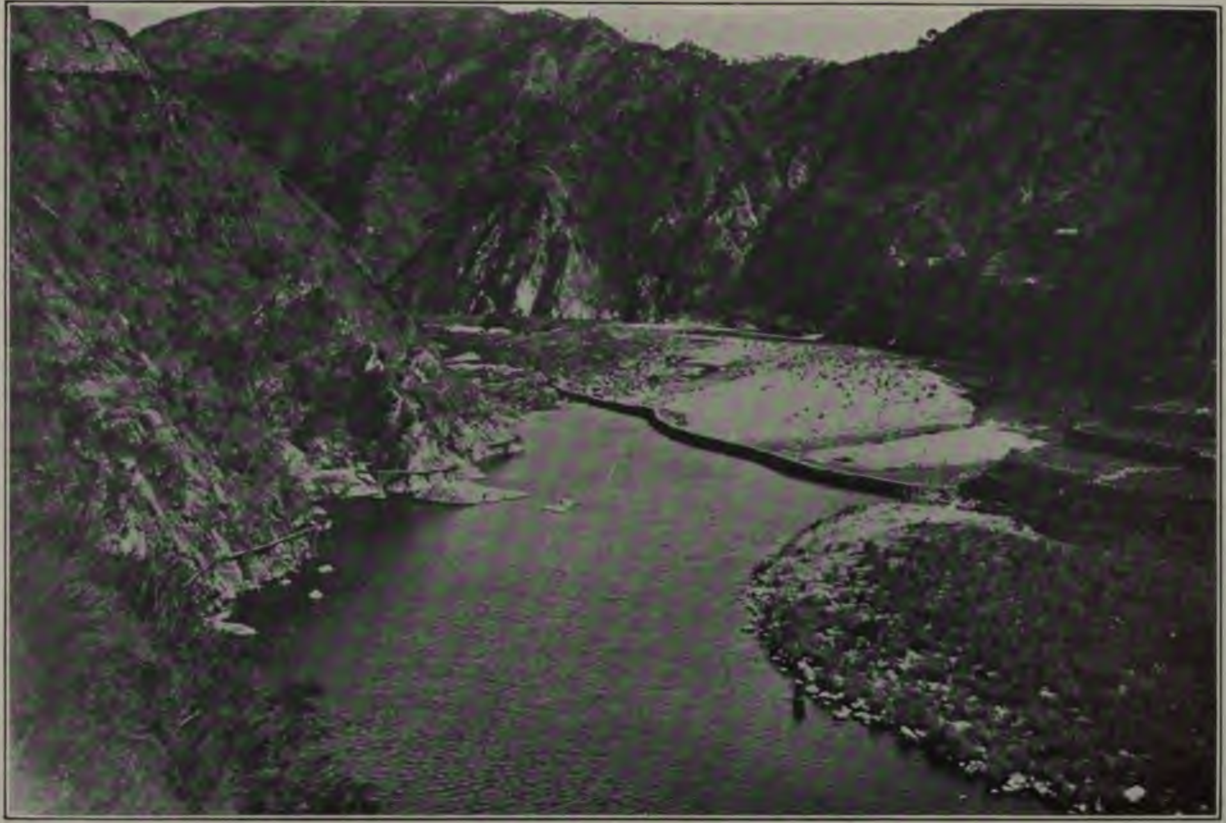

PLATE I.

PLATE II.

A CASE OF INFANTILE BERIBERI WITH AUTOPSY REPORT.[1]

By **José Albert.**[2]

The case under discussion is that of an infant three months of age, which was brought to my clinic at St. Paul's Hospital on the afternoon of December 3 last, and died during the next night. Upon examining the child, she was seen to be of robust frame. In general the face was pallid, but cyanosis was present around the mouth and nostrils. There was no rise of temperature; œdema of the legs and anterior chestwall was present; the urine was scanty; nausea was present, but not vomiting. From the previous afternoon until the time she was examined, two normal stools had been passed; the respirations numbered from 30 to 40, and the pulse 120 to 130 beats per minute. Pronounced aphonia was present, although the patient was constantly moaning.

The history of the case as given by the mother is as follows:

Two weeks previously the child lost her voice, as the result, so the mother thinks, of a bath. She vomited a good deal at this time and had frequent stools of a very dark color. It was these gastric and intestinal symptoms which caused the mother to bring her to the hospital.

Upon examining the mother, it was seen that she was suffering from a dropsical form of beriberi. There was œdema and swelling of the feet, the patellar reflexes were absent; there was a sensation of weight in the epigastrium; tachycardia was present. The mother said she had suffered from beriberi for a long time; she had besides the present child four other children of whom the first three, all of whom she had nursed, had died during the first months of infancy. The fourth child, immediately preceding the one whose case I am reporting, was not suckled, but had been brought up by the bottle, and is alive and in good health.

With the foregoing data there could be no doubt that the case was one of beriberi. As has already been mentioned above, the child died a little more than twenty-four hours later, and the autopsy and microscopical examination for the results of which I am indebted to Drs. Marshall and Gilman showed that the most important lesions were:

First, degeneration of both vagi and swelling of the cells of the right cervical ganglion; second, dilatation of the right side of the heart to a degree which threw it forward in contact with the sternum; third, collection of fluid in the pericardium; fourth, hæmorrhagic areas in both lungs; fifth, subcutaneous œdema in the legs and chestwall.

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[1] Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, February 29, 1908.

[2] Professor of pediatrics in the Philippine Medical School.

As is seen, these lesions correspond exactly to those found in adults affected with the pernicious or cardiac form of beriberi, and the statement of Hirota, of Tokyo, to the effect that infantile beriberi is symptomatically and pathologically identical with the acute cardiac form in the adult is again born out.

The full report of the autopsy findings is as follows:

Autopsy.—Body of Filipina infant 56 centimeters long. Rigor mortis absent. Very little œdema of ankles. Slight œdema over chest. No œdema of face or hands. The subcutaneous fat is moderately abundant and firm. The peritoneal cavity is dry. The peritoneal surfaces are smooth and glistening. There is no injection along the vessels leading to the umbilicus. The diaphragm reaches the 4th space on the right side and to the fifth rib on the left. The thymus gland extends to a normal distance on top of the pericardium. There is a small amount of clear fluid in each pleural cavity.

Heart: The right auricle is considerably dilated; a post-mortem clot is found inside the right auricle. The tricuspid valves are normal. The left ventricle is small. The mitral valve and aortic valve are normal. The surface of the heart is pale; the muscle is firm. The length of the heart from the auriculo-ventricular groove to the apex is 4.5 centimeters. The walls of the left ventricle average 4 millimeters and of the right 4 millimeters in thickness. At the base of the aorta there are a few hæmorrhagic points beneath the pericardium, but no ecchymosis beneath the epicardium.

The *left lung* is moderately voluminous and shows few ecchymoses beneath the pleura. The color is mottled, pale, and red. The consistence, fairly firm. On section the lung is pale, uniform, and apparently normal. The hæmorrhagic points under the pleura correspond to small areas one-half millimeter in diameter extending into the substance of the lung.

The *right lung* is also moderately voluminous and shows a few hæmorrhagic points and in general resembles the left lung. On section it also appears normal. The lymph glands at the root of the lung also appear normal in size, consistence, and color. The omentum and mesentery contain very little fat. The contents of the duodenum is normal.

The *stomach* is small, contracted, and contains 5 cubic centimeters of thick, tenacious mucus mixed with a small amount of curded milk.

The *left kidney* measures 4 by 2 by 2 centimeters. The capsule strips readily, leaving a mottled surface. Post-mortem discolorations and traces of foetal lobulation are present. On section the cortex is dark brown and post-mortem change is evident. The structures are not clearly visible.

The *right kidney* measures 4 by 3 by 3 centimeters and presents the same general appearance as the left.

The *spleen* shows post-mortem change; it measures 5 by 3 by 2 centimeters. Its consistence is firm, the edges are sharp and the capsule smooth. On section the structures are clearly visible, the malpighian bodies being more conspicuous than normal. The pulp is firm and dark.

The *left suprarenal* is apparently normal, being pale yellow in color. On section the cortex is seen as a yellow-white band, with a pale, dark color.

The *trachea, larynx,* and *bronchi* are clear.

The liver measures 12 by 7 by 4 centimeters. Its consistence is firm, the edges are sharp, the color is mottled. On section there is a pale yellow area near the surface while the general color is a brownish red and opaque.

Intestines: The mucous membrane is pale. There are swollen areas in Peyer's patches in the lower portion of the Ileum.

Histological examination by Dr. Gilman.—Microscopically the heart shows a diffuse, cloudy appearance with some separation of the muscle fiber and in places rather an abundant infiltration of round cells.

The lungs show a slight œdema with a few red blood cells free in the alveoli in various areas. The bronchial glands are normal. The kidneys show early post-mortem degeneration. The glomeruli are generally congested, the tufts being packed with red blood corpuscles.

The spleen shows a marked grade of congestion; the malpighian areas appear smaller than normal and are widely separated by the pulp, the sinuses of which are markedly engorged with red corpuscles.

The liver is markedly congested and the cells forming the periphery of the lobules show quite advanced fatty infiltration.

Both vagi show swelling of the fibers with complete degeneration of about one-half of the nerve; the remaining fibers stained poorly and showed in areas a slight round cell infiltration.

A section of the right cervical ganglion shows a general swelling of the nerve cells and their nuclei with an eccentric arrangement of the latter. A few of the cells show a granular change in the protoplasm.

I have been led to present this report since, with the confirmation by autopsy of this case of infantile beriberi, that nosological entity acquires definitely and indisputably, a rightful place in the pathology and statistics of infantile mortality in the Philippines.

The discovery of the existence of beriberi in nursing infants is due to Professor Hirota, of Tokyo, who first published, in the "Centralblatt für Innere Medizin," in 1898, his studies on this condition which he began in 1888. Before the publication of his studies, such eminent authors as Baelz and Scheube denied the existence of beriberi in nursing infants. Even at the present time, Scheube is not convinced that nurslings may acquire beriberi from their mothers through the milk.

It may be said that the recognition of the existence of infantile beriberi in the Philippines is of rather recent origin, since it is only four or five years ago, and due to Scheube's work on tropical diseases, that the observations of Hirota became accessible to the Filipino physicians, especially through Drs. Luis and Manuel Guerrero. But our clinical recognition was little more than a mere suspicion, as it had not been confirmed by a pathological demonstration on the cadaver as in the present case. Dr. Herzog, of the biological laboratory of the Bureau of Science, in Manila, who published in 1906 a most thorough research on beriberi, was not able to adduce a single autopsy on a case of beriberi in a nursing infant, undoubtedly because there had been no opportunity to perform one. He therefore limited himself to admitting the existence of infantile beriberi and citing the clinical testimony of the Filipino physicians.

How far infantile beriberi, acquired through nursing the mother, may or does increase mortality in the Philippines is a question to be reserved for the future. What may be confidently affirmed is that the best method of establishing a sound basis for the fight against infant mortality in the Philippines is to commence by revising the form of death certificate used for infants of less than one year in such a manner as to have a statement on the death certificate of each infant under one year of age dying in Manila, of the kind of nourishment which the infant has received during life, as is the practice in many other countries.

EDITORIAL.

DYSENTERIC ABSCESS OF THE LIVER.

The passing of abscess of the liver among Americans in the Philippines is so apparent from recent available statistics, that this most dreaded and most serious complication of intestinal amœbiasis should soon to a great extent lose its terrors, at least for Americans. During the interval from 1901 to 1905 the writer operated on about 100 cases of this form of abscess in both military and private practice, and 95 per cent at least of the patients were Americans; the percentage of recoveries was about 90 per cent. Exact data are not now available. The following operations were performed in St. Paul's Hospital, Manila.

Operations for amœbic abscess of the liver, St. Paul's Hospital, Manila.

Year.	Cases.	Americans.	Europeans.	Japanese.	Negroes.	Filipinos.
1905	9	5		3	1	
1906	8	2	2	1	1	2
1907	7	3				4
1908	2		1	1		
Total	26	10	3	5	2	6

The admission to the hospital of all classes of cases during this period was over 7,000.

A number of cases of liver abscess have been treated in the military and other hospitals of Manila during these years and a marked recent decrease of the disease among Americans is shown by the records of these institutions as far as could be learned. These figures prove in a most striking manner the efficacy of rational treatment of amœbic disease of the colon. But a short time ago, the discovery of amœbæ in their stools came as such a shock to sensitive patients that the overcoming of the dread and depression following the discovery of the parasites was no small part of the treatment.

Dr. Vassal, in connection with the above table gives the following details furnished by Dr. Gaide, senior major surgeon of colonial troops, Hanoï, Tonquin.

> Although suppurating hepatitis is not rare at Hanoï, the greater part of the patients treated for this trouble at the military hospital of the city come from different parts of the upper country invalided for paludisine, dysentery, or some other trouble, hepatitis appearing only after their arrival at Hanoï, or they were sent because of this trouble by ambulance to the hospital at Hanoï, in order to be operated on under the most favorable conditions.
>
> In the course of the last four years the proportion of the mortality in every 100 patients treated has been as follows: 28 per cent in 1904; 29 per cent in 1905; 26 per cent in 1906; 34 per cent in 1907.
>
> The mean mortality per 100 patients treated, calculated for the four years indicated above, reaches the average of 41 in 100.

Dr. R. D. Keith, of the Straits and Federated Malay States Medical School, Singapore, Straits Settlements, has sent us the following table for Singapore:

Consecutive records examined, 1,564;[a] *dysentery present in 300 cases.*

Race.	Number of cases of dysentery.	Amœbiasis.	Abscess of the liver.[b] [c]
Chinese	270		14
Tamils	20		1
Malays	2		
Europeans	2		2
Other races	6		
Totals	300	194	17

[a] These members correspond to about 15,000 cases in the hospitals.

[b] The dysenteric condition in the seventeen cases was as follows: 6 advanced, 4 marked, 6 slight, 1 very slight. The small intestine was affected as well as the large in 4 out of the 17 cases.

[c] Single abscess occurred 5 times; multiple abscess 12, the right lobe alone was affected 11 times; the left lobe alone 1 time; both lobes were affected 5 times.

JOHN R. MCDILL.

THE FREE DISPENSARY OF THE PHILIPPINE MEDICAL SCHOOL.

The free dispensary of the Philippine Medical School was organized in September, 1907, the necessary rooms, pending the construction of the new building in connection with the Philippine General Hospital, having been furnished by the authorities of St. Paul's Hospital, Manila. This clinic, from the beginning, has been markedly popular with the people and has furnished abundant material for the purposes of instruction.

The attendance for the nine months, up to and including June 30, 1908, is given in the following table:

Month.	Medical.	Surgical.	Children.	Obstetrical.	Eye, ear, nose and throat.	Totals.
1907.						
September	492	236	73	2	19	822
October	575	254	43	1	101	974
November	587	281	56	1	155	1,080
December	508	286	70	1	160	1,025
1908.						
January	573	324	45	0	221	1,163
February	577	331	37	0	223	1,168
March	605	361	43	0	265	1,274
April	494	326	43	0	251	1,114
May	413	301	44	0	179	937
June	620	388	83	0	221	1,312
Totals	5,444	3,088	537	5	1,795	10.869

The months of July and August have shown even a greater number of patients and, with careful records, this clinic should in a short time furnish valuable data for a more extended study of the diseases existing among the poorer classes in Manila and the provinces.

PAUL C. FREER.

REVIEW.

Pharmacology: The Action and Uses of Drugs. By Maurice Vejux Tyrode, M. D. Cloth. Pp. ix + 255. Price, $1.50 net. Philadelphia: P. Blakiston's Son & Co., 1908.

It is to be presumed that this work is for the use of students of medicine and that consequently the author has endeavored to reduce the limits of the book so that it can be used for ready reference. In so doing he has omitted altogether the experimental side of pharmacology and so we are brought back to former times, when the knowledge of pharmacology possessed by beginning practitioners was based on the more or less positive statements of the text-books they had read and the lectures they had heard. It is our belief that the text-books of pharmacology for beginners should be so constructed as to include experimental work and at least general laboratory directions, that they should handle but few drugs, and these well chosen and that the topic of materia medica had best be reserved for a separate volume.

It is to be regretted, also, that the author has not included, so far as expedient and necessary, structural chemical formulæ. The mere name of a drug, even to those thoroughly conversant with the subject of pharmacology, often conveys no meaning, where the chemical formula does.

This book, however, is a short compendium which doubtless will find its place in the class room, although the student should be encouraged to do much collateral reading in connection with it.

P. C. F.

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A STUDY OF THE PRECIPITIN AND COMPLEMENT FIXATION REACTIONS.

By HARRY T. MARSHALL and OSCAR TEAGUE.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

It is well known that if red corpuscles are treated with an inactivated, specifically hæmolytic serum, together with a fresh serum containing complement, the corpuscles are dissolved. No hæmolysis is produced if the fresh serum is not added, or if it contains no free complement. Any procedure which removes the free complement will therefore prevent hæmolysis, and, conversely, we can determine whether any given treatment of a fresh serum removes free complement from it by performing the hæmolysis test with it after such treatment. It is clear from this that the occurrence or non-occurrence of hæmolysis may be used as the indicator of the presence or absence of free complement in the fresh serum.

If serum containing free complement is present when a bacterial extract is mixed with the corresponding antibacterial serum, among other changes occuring, some reaction takes place, in the course of which the free complement disappears. The nature of the reaction and what becomes of the complement is not known, but the indicator described above proves conclusively that there is no complement remaining free after the reaction has taken place.

It has been found that this is a general reaction, which according to some observers, occurs whenever complement is present during the union of any specific antigen and antibody, or according to others, during the union of any specific antigen with its corresponding precipitin. There are also a number of other agencies which are not specific, but which lead to the disappearance of complement.

It can be seen from what has preceded, that for the specific complement deflection phenomenon we require:

1. A hæmolytic complex consisting of (*a*) specifically hæmolytic serum, (*b*) corresponding homologous red blood corpuscles.
2. Fresh serum containing free complement.
3. An antigen.
4. An antibody specific for the antigen.

If 2, 3, and 4 are brought together for an hour and are then added to 1, no hæmolysis occurs as the complement in 2 has been "deflected" during the union of 3 and 4. Knowing that this reaction always occurs, the phenomenon can be used for purposes of diagnosis, either of the antigen, (3), or of the antibody, (4).

The deflection test has been applied to three main subjects:

I. In the diagnosis of syphilis.

II. To supplement the precipitin reaction in the forensic diagnosis of minute traces of blood, and in the differentiation of blood of various species and subspecies.

III. In the diagnosis of bacteria and of bacterial diseases.

In a former paper one of us (Marshall(1)) traced the origin and development of the deflection method. The present article will deal in detail with (1) the technique and its modifications, (2) the interpretation of positive and negative results, (3) the range of application of the method, (4) its diagnostic value, and (5) lipoidal and non-specific deflections. We will also describe a comparative study of this and the precipitin method.

I. TECHNIQUE FOR THE SERUM DIAGNOSIS OF SYPHILIS.

1. Preparation of Materials.

A. THE HÆMOLYTIC COMPLEX.

a. The hæmolytic serum.—All observers have used the serum of rabbits immunized against the erythrocytes of sheep. Wassermann, Neisser, Bruck, and Schucht(2) recommend using a serum of which from 0.001 to 0.002 cubic centimeters dissolves 1 cubic centimeter of a 5 per cent suspension of sheep's corpuscles when treated with 1 cubic centimeter of a 0.1 dilution of guinea pig serum. Of this he used twice the exact dissolving dose with each cubic centimeter of 5 per cent sheep's corpuscles. Meier(3) and Michaelis and Lesser(4) use and recommend three times the exact dissolving dose of amboceptor.

Wassermann(2) remarks that the limits of the hæmolytic amboceptor must be determined from time to time. The avidity of complement for the amboceptor varies with the particular immune serum. When the serum grows old, it of itself causes deflection and under these circumstances it can only be used by treating the corpuscles with it and then centrifugating and suspending the corpuscles in fresh salt solution before adding complement.

b. The red blood corpuscles.—The authors quoted(2) note that the corpuscles must come from a healthy sheep which has not been bled too frequently. After frequent bleedings, the corpuscles become too fragile for use. The blood must be defibrinated, and the corpuscles washed and centrifugated until entirely free from serum, and a 5 per cent suspension made in 0.85 per cent salt solution.

c. The complement.—The complement, according to the same authors(2), must be serum obtained from guinea pigs on the day of the experiment; the serum must be free from hæmoglobin and must be centrifugated until perfectly clear.

b. ANTIGEN.

Wassermann(2) uses extracts in salt solution from various organs of infants who have died of congenital syphilis, made by taking 1 gram of organ, grinding thoroughly in a mortar with 4 cubic centimeters of 0.85 per cent salt solution, plus 0.5 per cent carbolic acid, shaking for twenty-four hours, and centrifugating until the fluid is perfectly clear. He uses 1 cubic centimeter of a 0.1 dilution of this extract for each test tube.

Meier(3) employs only extracts of livers from syphilitic fœtuses, as other organs are less active.

Morgenroth and Stertz(5) suggest that the luetic organs be frozen and kept solid until ready for use, and that from these frozen organs one gram be used for each experiment in preparing a fresh extract.

Marie and Levaditi(6) thoroughly desiccate the fœtal organs and make a powder which retains its strength for months, and for each experiment make up a fresh extract with a little of this powder and salt solution.

The extract of Wassermann is fit for use for about six days, although Meier(3) finds that an ordinary aqueous extract retains its strength for four months if protected from heat, light and air, and if not too frequently centrifugated.

C. THE ANTIBODY.

The antibody is usually obtained from the serum of a patient suspected of suffering with the disease. In a large number of cases the cerebro-spinal fluid has been employed as antibody. Meier(3) draws 6 or 8 cubic centimeters of blood and as quickly as possible obtains at least 1.4 cubic centimeters of serum which is inactivated at once. In the case of children, less blood is drawn, also a smaller quantity of spinal fluid is used. He recommends that the serum or spinal fluid be used immediately because of the danger of rapid deterioration upon standing. In establishing the value of the sero-diagnosis of syphilis Wassermann(2) uses the serum of monkeys first inoculated with syphilis and subsequently treated with subcutaneous inoculations of syphilitic material. He always clarifies the serums and extracts at as short an interval as possible before performing the experiment. Meier finds also that the serum rapidly deteriorates and either loses its deflecting power, or, more usually, causes deflection even with extracts of normal organs.

There are various precautions to be observed in regard to both antigen and antibody. Wassermann and his colleagues(2) make the following observations:

1. Many extracts and serums of themselves alone pick up complement, the amount of extract or serum required varying with the individual preparation and in the case of each, varying with age; 0.1 cubic centimeter of a serum may not block when it is fresh, but after standing it will do so.

2. Any extract or serum showing even the slightest trace of cloudiness or precipitation will deflect and is unfit for use until centrifugated.

3. Frequently a serum or extract which is perfectly clear, absorbs complement. This is especially true of those which have stood long before being clarified by centrifugation or before inactivation.

To avoid this non-specific deflection of complement centrifugate and inactivate immediately after obtaining the serums and extracts; preserve carefully under aseptic precautions in completely filled tubes, closed by fusing the glass, and keep at a constant freezing temperature away from light and air; centrifugate as frequently as is necessary; determine in each individual experiment the non-deflecting dose, and never use a large one.

4. Wassermann and Citron(7) have shown that albumoses, glycogen, fatty stuffs, and lecithin block complement in even small doses. The richer a fluid is in colloidal materials, the more it deflects and vice versâ. Extracts of red blood corpuscles deflect most; spinal fluid, least. As a rule, fresh red blood corpuscle extract does not deflect in a dose of 0.5 cubic centimeter; old extracts deflect in doses no larger than 0.1 cubic centimeter. These various effects are distinct from the specific deflection.

Michaelis and Lesser(4) find that occasionally an extract of syphilitic liver is itself hæmolytic when added to corpuscles, amboceptors and complement. Furthermore, a definitely deflecting serum will often suddenly lose its power after standing.

Meier(3) finds that antibody loses strength upon being kept even in completely filled, tightly sealed and blackened tubes in a cold place. Its action also varies with the age and condition of the complement and of the red blood corpuscles. Wassermann(2) notes that upon standing, even a perfectly clear serum or extract gradually develops a cloudiness or even a slight precipitation. It is very necessary to centrifugate both serum and extract until they are perfectly clear before performing the experiment. The slightest trace or precipitation in the serum makes it unavailable for the experiment. It must be remembered, however, that each centrifugation of a serum or extract decreases its strength, it appearing that the active constituents are carried down in the sediment.

2. PRELIMINARY EXPERIMENTS.

A. COMPLEMENT.

Most observers, including Wassermann(2), Michaelis(4), and Meier(3) recommend the use of 1 cubic centimeter of a 0.1 dilution of guinea-pig serum, as the standard amount of complement for use in each test.

B. VALUE OF HÆMOLYTIC AMBOCEPTOR.

With each amboceptor a test must be made at the outset to determine approximately its value. This value remains fairly constant, but shows gradual and progressive deterioration. Before each experiment make a preliminary test with 0.1 cubic centimeter of guinea-pig serum to determine whether the hæmolytic amboceptor retains its strength.

Meier(3) simplifies this experiment as follows: He heats diluted fresh complement for one hour at 37°, so that the results obtained will be comparable with those in the rest of the experiment; he then prepares three test tubes with fixed amounts of corpuscles and the heated complement, and dilutions of 1.5, 2 and 3 of the amount of the hæmolytic amboceptor which proved satisfactory in the previous experiments. Thus, if in a previous experiment 1: 200 of amboceptor gave a good deflection, the dilutions of hæmolytic amboceptor tried out in the preliminary experiment will be 1: 300, 1: 400, and 1: 600. He examines this preliminary test after fifteen minutes, thirty minutes, one and two hours. In the first tube he expects to find lysis after thirty minutes, in the second in one hour at the latest, in the third it should be almost complete in two hours. After the first two tubes are positive, he estimates the dose of amboceptor which will be required and continues with the deflection experiment without delay.

C. ANTIGEN.

Meier(3) notes that it is very necessary to test the value of the antigen and to employ fresh serum from an unquestionably syphilitic patient in making the test. If the syphilitic serum is not fresh it may deflect with an extract of normal organs. Wassermann and Plaut(8) note that the aqueous extract undergoes sudden and rapid alterations in deflecting power. This is confirmed by others including Morgenroth and Stertz.

D. FINAL PRECAUTIONS.

In a preliminary test determine that the suspected serum does not cause deflection with normal extract. If there is enough serum available, test its action upon sheep's corpuscles with complement. Human and monkey serum, normal or luetic is often quite strongly hæmolytic for sheep's corpuscles, at times 0.1 cubic centimeter producing hæmolysis of 1.0 cubic centimeter of a 5 per cent suspension.

The test tubes, glassware and other apparatus must be irreproachably clean, the extracts and serums must be collected and preserved under aseptic precautions, and the experiments must be conducted in such a way as to avoid contamination by bacteria, dust, etc.

3. Details of the Actual Experiment.

a. Amounts of materials.—Wassermann, Neisser, Bruck, and Schucht(2) use 0.1 cubic centimeter of each one of the ingredients, bringing the total volume in each test tube up to 5 cubic centimeters with normal salt solution. Meier(3) dilutes his materials so that he needs only to measure out 1 cubic centimeter of each ingredient, making the volume constant with salt solution. He uses two quantities, 0.2 and 0.1 of the antibody and also of the antigen. Michaelis(4) and others also use 0.2 or 0.1 of serum from the suspected case with 0.1 or 0.2 of extract of syphilitic organs. Landsteiner and Stankovic(9) use 10 parts of 0.8 per cent salt solution; 1 part of serum inactivated at 56° for one-half hour; 1 or 2 parts of extract and 1 part of guinea-pig complement. After one hour at 37° they add 1 part of 50 per cent sheep's corpuscles suspension free from serum and previously treated with two dissolving doses of hæmolytic serum, incubate for one hour and a half at 37°.

Morgenroth and Stertz(5) recommend wider variations in the amounts of substances employed, especially of the antigen. They show that the zone within which deflection occurs is narrow, in one experiment cited deflection occurring when 0.001 to 0.0025 of antigen was employed, but failing to occur with greater or less amounts.

In most of the literature, 0.1 cubic centimeter of the extract of antigen was employed in each test tube. Meier(3) finds that this usually suffices when mixed with 0.1 cubic centimeter of the luetic serum, while it produces no deflection with 0.2 cubic centimeter of normal serum. If the extract of antigen is weaker he uses from 0.2 to 0.4 cubic centimeters with 0.1 cubic centimeter to 0.2 cubic centimeter of the luetic serum, always making a control to prove that the same dose of extract produces no deflection with even twice the dose of normal serum.

Meier(3) notes that the antibody varies quantitatively in different cases and the quantitative test is necessary for exact scientific work. In practice, however, it is necessary to use only two dilutions, neither of which is so strong as a control with normal serum need be in order that the normal serum produces deflection. In practice Meier uses a dilution of one in five of antibody, that is 0.2 cubic centimeter for one quantity and for the other one-half of this, viz, one part in ten, or 0.1 cubic centimeter of antibody, but in a few of his cases 0.005 cubic centimeter (=1: 200) of serum, deflected completely when mixed with luetic extract, while even 20 times the amount (0: 1 cubic centimeter) gave complete lysis, i. e., no deflection, when mixed with extract of normal organs.

Michaelis and Lesser(4) also employ about 0.2 cubic centimeter of serum from the patient.

It is generally customary among all authorities to use 1 cubic centimeter of a 0.1 dilution of complement as a standard dose.

The total volume of fluid employed by different authorities varies from 2.5 to 10 cubic centimeters.

b. Time and temperature.—The general advice given by Wassermann with regard to time and temperature is to allow the antigen, antibody and complement to remain in contact for one hour at 37°, subsequently allowing this mixture to act upon the hæmolytic complex for two hours at 37°. Some authorities allow antibody, antigen and complement to remain at room temperature. The result may be observed upon removing the test tubes from the incubator, or they may be placed on ice and the result noted on the following morning.

Meier(3) thinks it is very important to observe closely the experiment in the incubator and not let it run automatically for two hours. As soon as lysis is complete in all of the controls, remove the test tubes from the incubator and put them on ice without waiting for the expiration of two hours. Frequently from three-quarters to one hour suffices, especially if the corpuscles and hæmolytic amboceptor have been previously mixed for one-quarter to one-half an hour. This is a great improvement, and does away to a large extent with the "Nachlösung" or hæmolysis which develops in some test tubes after being removed from the incubator and placed upon ice. It is even better to bind hæmolytic amboceptor to the corpuscles by allowing them to stand in contact for one-half hour, and remove the excess of serum by centrifugation and suspend the laden corpuscles in fresh salt solution.

c. Controls.—The controls which are required in conducting this experiment are numerous. In addition to the preliminary tests mentioned above, each experiment must be accompanied by the following controls.

A parallel series of tests must be made—

1. With the serum under examination and normal extract. In these controls there should be no deflection; if deflection occurs, it is not specific and the experiment must be thrown out.

2. With standard fresh syphilitic serum and the extract of syphilitic liver. In this control there should be definite deflection, otherwise the extract is defective, and the experiment fails.

3. With standard fresh syphilitic serum and extract of normal liver. In this control there should be no deflection. If it occurs either the standard serum is deteriorating or the total quantity of colloids is sufficient to produce a non-specific deflection.

4. With serum which is certainly not syphilitic and the luetic extract. In this control there should be no deflection. If it occurs the experiment is valueless and a fresh luetic extract must be prepared.

5. With the antibody serum and complement alone. This test should give no deflection.

6. With the luetic extract and complement alone. This test should give no deflection.

7. With the red corpuscles, hæmolytic amboceptor and complement, which has been previously heated to 37° for one hour. In this control there should be complete hæmolysis.

8. With blood corpuscles in salt solution alone.

9. With blood corpuscles and hæmolytic amboceptor alone.

10. With blood corpuscles and complement alone.

11. With blood corpuscles and organ extract alone. In these controls there should be no hæmolysis.

Meier(3) remarks that as experience increases, it becomes less necessary to make daily controls of the standard luetic serum with extracts and of serums without extracts, for fresh serum in 0.2 cubic centimeter quantities never deflects alone, but on the contrary, increases the rapidity of lysis because of the amboceptors for sheep's corpuscles contained in normal and luetic human serum. The only exception to this rule is that the serum from an animal which has just had a hearty meal may cause deflection and under any circumstance this serum is not useful because of its milkiness. All authorities agree upon the necessity of having these various controls.

d. Tables.—The following tables from various authorities illustrate the manner of setting the deflection test for the determination of the antibody content of the suspected serum.

Wassermann, Neisser, Bruck and Schucht(2) give the following summary of one of their experiments:

Immune serum:

Obtained from a monkey inoculated and subsequently immunized with syphilitic material.

Antigen:

1. Extract of organs from an infant with congenital syphilis.
2. Extract of bone marrow of a monkey killed seven weeks after inoculation with syphilis.

Antigen controls:

1. Extract of organs from a non-syphilitic fœtus.
2. Extract of bone marrow of a monkey free from syphilis.

TABLE I.

1	0.1 immune serum.	0.1 extract luetic fœtus.	Fresh guinea pig complement 0.1.	Union for 1 hour at 37°.	0.002 rabbit serum hæmolytic for sheep corpuscles (2 dissolving doses).	1 c. c. of 5 per cent suspension of sheep's blood.	Blocking of hæmolysis.
2	do	0.1 extract luetic monkey.	do	do	do	do	Do.
3	do	0.1 extract normal fœtus.	do	do	do	do	Complete hæmolysis.
4	do	0.1 extract normal monkey.	do	do	do	do	Do.
5	0.1 normal monkey serum.	0.1 extract luetic fœtus.	do	do	do	do	Do.
6	do	0.1 extract luetic monkey.	do	do	do	do	Do.
7	0.1 immune serum.	Salt solution	do	do	do	do	Do.
8	0.1 normal monkey serum.	do	do	do	do	do	Do.
9	Salt solution	0.1 extract luetic fœtus.	do	do	do	do	Do.
10	do	0.1 extract luetic monkey.	do	do	do	do	Do.
11	do	0.1 extract normal fœtus.	do	do	do	do	Do.
12	do	0.1 extract normal monkey.	do	do	do	do	Do.

The other controls which are not tabulated are: (1) the hæmolytic system alone; (2) blood corpuscles in salt solution; (3) blood corpuscles with complement alone; (4) blood corpuscles with hæmolytic amboceptor alone; (5) organ extract with blood corpuscles.

The volume of fluid in each tube is brought up to 5 cubic centimeters with salt solution.

In this table, numbers 1 and 2 are the only tubes showing the real experiment, all of the others, including the five noted below the table, being employed as controls. These two tubes demonstrate that there is specific luetic material in the organ extracts made from the syphilitic fœtus and the syphilitic monkey, and that there are specific luetic antibodies in the serum of the immunized monkey.

Wassermann, Neisser, Bruck and Schucht(2) also use a simple form of table indicating only the combinations which are brought together in the presence of complement serum, together with the final result upon hæmolysis.

TABLE II.

[Wassermann, Neisser, Bruck and Schucht; Table I modified.[1]]

Serum of normal monkey.	Serum of luetic monkey.	Extract of non-luetic child's liver.	Extract of luetic child's liver.	Result.
----------	0.1	----------	0.1	Blocking of hæmolysis.
0.1	----------	----------	0.1	Complete solution.
----------	0.1	----------	----------	Do.
----------	----------	----------	0.1	Do.
----------	0.1	0.1	----------	Do.

Meier(3) uses the following table to indicate whether a suspected serum "A" contains antibodies, which will produce deflection with a syphilitic extract and with no other. In this table the actual experiment is shown in column I, numbers 1 and 2, while the other tests are controls. In the last column is recorded the degree of deflection.

He does not tabulate the hæmolytic system with its controls.

TABLE III.

Serum.	Amount.	I.		II.		III.		End result.
		Luetic extract.	Result.	Extract of normal organs.	Result.	Salt solution.	Result.	
A	0.2	0.2	Complete blocking.	0.2	Complete solution.	1.0	Complete solution.	Serum A = ++++ is a syphilitic serum.
Do	0.1	0.1	do	0.2	do	1.0	do	
Standard syphilitic serum.	0.2	0.2	do	0.2	do	1.0	do	
Normal serum	0.2	0.2	Complete hæmolysis.	0.2	do	1.0	do	
----------	----------	0.4	----------	----------	----------	1.0	do	
----------	----------	----------	----------	----------	----------	1.0	do	

A = Serum to be tested.

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[1] *Ztschr. f. Hyg. u. Infectionskrankh.*, Leipz. (1906), **55**, **455**.

Instead of recording the presence or absence of hæmolysis and its degree, Meier uses two quantities of antibody 0.1 and 0.2 cubic centimeter and follows Citron's scheme of interpreting the result directly in terms of deflection without first noting hæmolysis. The degree of deflection varies according to the combination of results obtained with these two quantities as follows:

Serum.		Designation of strength of reaction.
0.2.	0.1.	
Complete blocking	Complete blocking	+ + + +
Do	Incomplete blocking	+ + +
Do	Lysis	+ +
Incomplete blocking	do	+

4. MISCELLANEOUS.

Mühsam(10) notes that the negative test must be repeated after several days as the complement binding substances are not always constant in amount, and Wassermann(2) states that any specific serum, which of itself precipitates human albumen, is useless for the deflection test. This refers to the serum of monkeys previously immunized with luetic substances.

II. TECHNIQUE OF DEFLECTION TEST IN FORENSIC PRACTICE AND IN THE DIFFERENTIATION OF BLOOD.

The application of the deflection test for this purpose is essentially the same as in the case just considered. The known quantities are usually the hæmolytic complex, the complement serum, and the specific antibody obtained by immunizing a rabbit with human serum or other known material. The unknown quantity is the antigen, usually a blood clot or blood stain.

Neisser and Sachs(11, 12, 13) adopted the following technique in diagnosing blood clot or blood stain. They employ as the hæmolytic complex a 5 per cent suspension of sheep's corpuscles freed from serum, and the serum of a rabbit immunized against ox corpuscles which is always strongly hæmolytic for sheep's corpuscles also. The serum is completely clarified by centrifugation and inactivated by heating to 56° for half an hour.

The antihuman serum should be of such a strength that 0.01 cubic centimeter will deflect when treated with 0.0001 of human serum. In general they recommend of such a serum the use of 0.02 cubic centimeter as a basic amount for future work and further(12) that the amount of human serum used in the test should be small, 0.0001 being a good dose for testing.

In the deflection experiment, they(11) use 1 cubic centimeter of a 5 per cent suspension of serum-free sheep's corpuscles in 0.85 per cent salt solution treated previously with 0.0015 of hæmolytic serum, which is just twice the lytic dose. In other test tubes quantities of human serum varying from 0.01 to 0.000001 are mixed 0.1 of antihuman serum and 0.05 of guinea-pig serum;[2] after standing for an hour these tubes are treated with the sheep's corpuscles previously laden with amboceptor. The mixture is placed in the incubator two hours, transferred to ice, and the results noted in the morning.

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[2] In a later report they use 0.1 cubic centimeter of guinea-pig serum.

In testing blood stains in their three forensic cases, they(12) made extracts of the stain with normal salt solution using very small amounts of the solution.

The work of Neisser and Sachs has been repeated and its value tested by Schütze(14), by Bruck(15, 16, 17) and by Bauer(18).

The antisheep serum used by Schütze(14) is of such a strength that 0.0005 to 0.00033 cubic centimeter dissolves 3 cubic centimeters of 5 per cent suspension of sheep's corpuscles when treated with 0.1 cubic centimeter of fresh guinea-pig serum. He(14) immunizes rabbits either by intravenous inoculation of 3 cubic centimeters of human blood repeated three times or by subcutaneous inoculation of 8 or 10 cubic centimeters repeated five times. One week after the last inoculation the blood is drawn from the animal, the serum placed upon ice to clear, after which it is centrifugated and inactivated for one-half hour at 55°.

He makes his various dilutions in such a manner that the required amount of each constituent is contained in the volume of 1 cubic centimeter, the total of volume in each test tube being brought up to 5 cubic centimeters with salt solution.

Bruck(16) immunized rabbits by intravenous inoculations of 2 to 3 cubic centimeters of serum repeated after eight day intervals and the blood was drawn a week later. Of this serum 0.1 cubic centimeter usually precipitated the homologous antigen in a dilution of 0.1 or 0.05. With such a serum he could differentiate between the blood of the European, Chinaman, Arabian, Malay and monkey, by definite quantitative differences obtained in the reaction.

In differentiating between the serums of various human races two inoculations of the rabbits gave such a strength that using 0.1 of the serum with 0.1 of complement, deflection was obtained with 0.001 of the tested serum. Stronger serums gave doubtful results. Bruck emphasizes particularly the importance of using small doses for inoculating and immunizing the rabbits, so that only very low immunity is obtained. Acting upon this idea in a subsequent series of experiments, Bruck(16) immunized rabbits with 0.5 cubic centimeter every five days, giving three doses intravenously and ten days after the last dose withdrew the serum from the animal and tested it for its deflecting power. With this serum he could differentiate blood, pus and semen, from the same individual, using monkeys for obtaining the antigen for inoculation. In this test he used 0.1 of guinea-pig serum, 0.1 cubic centimeter of sheep's corpuscles plus two dissolving doses of hæmolytic serum, 0.1 cubic centimeter of antigen and a weak immune serum in dilutions varying from one-twenty-fifth to one-four hundredth.

The controls which are used vary according to the purposes for which the test is performed.

The general plan of the experiments of Neisser and Sachs, Bruck and Schütze with the controls and results are shown in the appended tables.

The following table, No. IV, of Neisser and Sachs(11) shows that the deflection is produced by human serum and that the reaction is specific, being given by no other serum except slightly by that of monkeys.

0.1 cubic centimeter of antihuman-rabbit serum+0.05 cubic centimeter guinea pig-serum+varying amounts of various normal serums as possible antigens+normal salt solution up to 1 cubic centimeter are brought together. After standing 1 hour at room temperature the mixtures are added to the hæmolytic complex = (0.0015 antiox-rabbit + 1 cubic centimeter 5 per cent sheep's red blood corpuscle suspension).

TABLE IV.

Amount of serum.	Hæmolysis produced with serum from—							
	Man.	Monkey.	Rat.	Pig.	Goat.	Rabbit.	Ox.	Horse.
.01	0	0	Complete	Complete	Complete	Complete	Complete	Complete
.001	0	0	do	do	do	do	do	Do.
.0001	0	Moderate	do	do	do	do	do	Do.
.00001	Trace	Complete	do	do	do	do	do	Do.
.000001	Complete	do	do	do	do	do	do	Do.
0.0	do	do	do	do	do	do	do	Do.

In this table the presence or absence of hæmolysis is noted. It must be remembered that deflection is indicated by the absence of hæmolysis, so that the first three or four tubes with human serum, and the first two with monkey serum are the only ones in which deflection has taken place.

The table of Schütze, No. V(14) shows deflection with human serum. The sheep's corpuscles and hæmolytic serum are mixed separately and not added until the other materials have been mixed and incubated for one hour at 37°.

TABLE V.

[Each ingredient = 1.0 cubic centimeter, total volume 5 cubic centimeters.]

Human serum.	Inactive anti-human serum.	Guinea-pig serum complement.	Antisheep serum.	Sheep corpuscles, 5 per cent.	Result.
.01	0.1	0.1	.002	5	Complete blocking of hæmolysis.
.001	0.1	0.1	.002	5	Do.
.0001	0.1	0.1	.002	5	Do.
.00001	0.1	0.1	.002	5	Appreciable blocking of hæmolysis.
.000001	0.1	0.1	.002	5	Hæmolysis.
.01+1 cc. salt sol.		0.1	.002	5	Complete hæmolysis.
0.0	0.1+1 cc. salt sol.	0.1	.002	5	Do.
0.0	0	0.1+2 cc. salt sol.	.002	5	Do.
0.0	0	0	.002+3 cc. salt sol.	5	No hæmolysis.
0.0	0	0	0	5+4 cc. salt sol.	Do.

TABLE VI.—*Comparison between fresh pig's serum and pig's blood dried on linen about three months.*

Pig's serum, or pig's blood spot.	Anti-pig serum.	Guinea-pig complement.	Anti-sheep serum.	Sheep corpuscles, 5 per cent.	Lysis.
Serum .01	0.1	0.1	.002	5	0
Serum .001	0.1	0.1	.002	5	0
Serum .0001	0.1	0.1	.002	5	0
Extract .01	0.1	0.1	.002	5	0
Extract .001	0.1	0.1	.002	5	Lysis.
Extract .0001	0.1	0.1	.002	5	Lysis.
Serum .01	0	0.1	.002	5	Complete.
Extract .01	0	0.1	.002	5	Complete.
	0.1	0.1	.002	5	Complete.
	0	0.1	.002	5	Complete.

Neisser and Sachs(13) and Schütze(14) call attention to the fact that the very sensitiveness of the test lays it open to error, and in testing for the specificity of a drop of blood on a piece of cloth, error may arise from the fact that the cloth may be contaminated by sweat or nasal secretion, or some other organic body substance. They therefore use as one control a test made with extracts from the cloth adjacent to the blood clot but free from blood.

Neisser and Sachs also used a control with boiled extract, as boiling removes the specific action of the serum deflection.

All tests in which there is evidence of bacterial action must be discarded(14).

Schütze(14) (Table VI) dried pig's blood on linen for three months and made a comparative test of this material with fresh pig serum with the deflection technique. One drop dried on a piece of cloth about 2 cubic centimeters in diameter dissolved in 2 cubic centimeters of salt solution and the extract cleared and filtered, had a deflecting strength of 0.01, while the fresh serum had a deflecting strength of 0.0001, the reaction being specific.

It is seen that there is an abundance of experiments which prove that when carefully performed, the deflection test is just as reliable as the precipitin test in differentiating between blood from different species, and that Neisser and Sachs, Schütze and Bruck, have found it possible to use it where the precipitin test is not available.

Neisser and Sachs recommend the adoption of the deflection test in forensic procedure, as a supplement to the precipitin reaction. They point out that it has certain advantages over the precipitin test which are: That it acts as a control for the precipitin method; that hæmolysis is a much more definite index than minute precipitation; that an opalescent serum is available for use; that it is not necessary to have such high potency serum as is needed in the precipitin test and that it is not necessary to wait for the clearing of the serum, which is so tedious in the older test.

They recommend in every forensic case in which the diagnosis of blood must be undertaken that the precipitin test be performed and upon its completion fresh guinea-pig serum (1.0 cubic centimeter of 1: 10 dilution) be added to each tube and the same materials be employed in making a deflection test.

Schütze agrees with Neisser and Sachs as to the value of the deflection test, while Bruck goes a step further. He recommends that the precipitin test be followed by a deflection test in which *moderately strong* immune serum is employed in order to obtain a racial differentiation, and thereafter a second deflection test be performed with *weak immune* serum for more delicate differentiation between the various body tissues or secretions.

INTERPRETATION OF RESULTS.

Clear cut results with satisfactory controls are received as conclusive by almost all observers. However, a large measure of confusion has been caused by the fact that some one or more controls are often omitted or because the resulting deflection is not as absolute as could be desired. When Wassermann first put forward this method he advanced the opinion that a positive result could be obtained only in the event of antibody and antigen uniting. The greater amount of work of this nature has been done in the investigation of suspected syphilitic serum, and up to the present time but few cases have been reported in which a positive result was obtained from a patient unquestionably free from infection. These few exceptions will be discussed later together with the change in the interpretation of the reaction which has been brought about by the rapid accumulation of fresh data. It may be stated that practically all investigators agree that the serum diagnosis proves more quickly and more certainly than any other method whether syphilis is or has been present. However, there are a number of other causes which produce deflection of a non-specific character. Bruck(15) reports that serum can be modified in its action by heat. Treatment at 55 degrees for half an hour usually reduces the power so that it is rare to obtain deflection with less than 0.3 cubic centimeter of such a serum. Normal monkey serum when heated for half an hour to 60 degrees acquires strong powers of deflection so that 0.1 will bind four times the dissolving dose of complement twice in succession, or in a single quantitative experiment will bind ten times the dissolving dose. Bruck compares this with the Pfeiffer-Friedberger reaction within the normal body. He finds that monkey serum is affected by heat in this manner with great regularity, guinea-pig serum less frequently, and rabbit serum still less. If the temperature is raised to 65° within 15 minutes the deflecting power is completely destroyed. He thinks it probable that the changes in deflection are due to molecular changes comparable to those occurring on long standing.

In the serum diagnosis of syphilis it has been frequently observed that a specific luetic serum will react with extracts of normal organs, particularly if a large amount of extract is employed. Even in this case, however, it is always necessary to employ a luetic serum in the test. Wassermann(19) was at first inclined to believe that this was a peculiarity of old extracts, but this does not seem to be the case.

A positive deflection may sometimes be observed in the control with an extract of liver itself, and Michaelis(4) also found that normal, non-deflecting serums may become deflecting after being kept frozen for a long time.

Bruck(17) found that his strong immune serum alone would cause deflection in the amount of 0.05 cubic centimeters, and Uhlenhuth(20) gives us a long list of substances of diverse nature which will produce non-specific deflection. Seligmann(21) concluded that absorption of complement is brought about by altering the molecular condition of the colloids in solution, even without causing precipitation. He states that his experiments do not explain the specific immunity reaction, but serve to show that there are other non-specific reactions of a similar nature.

Landsteiner(22) noted deflection when the syphilitic serum was used with extracts from the organs of normal animals, for instance, guinea-pigs' livers, or with alcoholic extracts of organs. We will describe below in more detail the nature of this process as well as the deflection with sodium oleate and lecithin.

However, the positive reactions which are not specific are of such a nature that they do not prevent a careful worker from employing the deflection method with a degree of certainty that is at least comparable to that attaching to many generally accepted clinical methods.

Although a positive fixation reaction with suitable controls give us certain evidence of the existence of syphilis, a negative reaction does not give the same proof of its non-existence. There are various possible sources of error which must be borne in mind in the interpretation of negative results.

According to Michaelis and others, the syphilitic extract of liver is occasionally hæmolytic itself. This function may more than compensate for any possible deflection; aqueous or alcoholic extracts of the liver are very unstable and it is not infrequent that a preparation which has proved satisfactory one day is perfectly useless on the next, and almost all extracts deteriorate on standing. There are also other possible causes which may lead to a negative reaction. They may be summarized as follows: (*a*) the patient has no syphilis and has never had it; (*b*) the patient has been completely cured of previous disease; (*c*) the serum is obtained from a patient during a temporary absence of the specific complement-binding substances from the blood of the patient; (*d*) there are certain refractory individuals whose serum always fails to deflect; (*e*) under energetic mercurial treatment it occasionally happens that the deflecting power disappears. It has also been observed that the reaction is less constant in the early stages and increases in regularity with the age of the disease.

The preceding discussion shows that the particular value of the deflection methods in clinical medicine at present is in the diagnosis of syphilitic diseases.

As Wassermann remarked(19) in December, 1907: "It is, up to the present time, more valuable than the Widal test was after an equal trial * * *. Probably as with the Widal test, some cases will be found which give a positive reaction, although there is conclusive reason to believe that syphilis is not present, but no such cases have been observed so far." He summarizes about 1,500 cases in which the serum diagnosis of syphilis has been attempted, in the great majority of which results were eminently satisfactory. Citron notes that in the primary stages 90 per cent were positive, in the secondary stage between 98 and 100 per cent, in the late cases where the process is active the reaction is practically universal.

The diagnostic value of the test has already been very great to the clinician, the surgeon and neurologist, and to other specialists, and Proskauer professes to employ it as a routine autopsy procedure.

The former article of Marshall(1) showed that there was considerable discussion over the theoretical interpretation of this reaction. Wassermann's idea that it indicated the union of syphilitic antigen with syphilitic antibody at first found almost universal acceptance.

However, Michaelis(23) very soon pointed out that the differences observed in the action of syphilitic serum toward syphilitic liver extract and toward normal liver extract were quantitative rather than qualitative. Then it was shown, as has been mentioned, that syphilitic serum gave positive reactions with extracts of normal organs, with lecithin and with sodium oleate and when comparative tests were made these substances yielded practically the same percentage of positive results as were obtained with the extracts of syphilitic liver. Hence the idea that the reaction was concerned with syphilitic antigen and antibody had to abandoned. Elias, Neubauer, Porges, and Salomon(24) regard the reaction as a precipitation reaction between colloids, the proteins of syphilitic serum having greater instability and yielding a wider flocculation zone than nonsyphilitic serum with certain hydrophilic colloids, such as extracts of organs, lecithin, sodium oleate, and sodium glycocholate.

Although the reaction is not specific in Ehrlich's use of the term, yet almost all observers agree that it has a high degree of clinical specificity.

Weil and Braun(25) report positive findings in pneumonia, typhoid, tuberculosis, diabetes, and malignant growths, but their results have not been confirmed by others. Much and Eichelberg(26) obtained positive reactions in 40 per cent of the scarlet fever patients subjected by them to the test. Seligmann and Klopstock(27), Hoehne(28), and Schliessner(29), however, report only negative results in scarlet fever. Wechselmann and Meier(30) and Eitner(31) obtained positive results in two cases of leprosy.

In contrast to the above exceptions, to which a few others could be added, the general verdict is that Wassermann's sero-diagnosis of syphilis is clinically specific.

We have thus far considered the application of the deflection of complement to the diagnosis of syphilis and to the differentiation of the blood of various species of animals. On treating the extract of bacteria with the serum of an animal immunized against the same bacteria, deflection of complement is likewise produced and the application of this principle bids fair to furnish an important addition to bacteriologic technique for the differentiation of closely related microörganisms.

The attempts of Ballner and Reibmayr(32) to differentiate the capsule bacteria and of Gengou(33) to distinguish between the acid fast bacilli by this method were unsuccessful. Schütze(34) concluded that the method was of no value in the study of cholera-like organisms, whereas Ruffner(35) claimed that it enabled him to differentiate between the strains of El Tor and of true cholera and was hence more delicate than the agglutination test. Leuchs(36) could distinguish between typhoid, paratyphoid and the colon bacillus and Vannod(37) between the meningococcus and gonococcus. Wollstein(38) obtained results contradictory to those of Vannod(37), but Teague and Torrey(39) were able to confirm Vannod's work and to show that furthermore differences such as Leuchs had found between typhoid and paratyphoid extracts exist between certain strains of gonococci. Kolle and Schatiloff(40) after having obtained negative results on using complement deflection in the study of experimental recurrent spirochætosis in mice and rats, finally obtained serum from a man suffering from the disease and with this were able to differentiate between the different varieties of spirochætæ.

Various attempts have been made to apply the method to the diagnosis of bacterial diseases by testing the serum of the patient against an extract of the bacterium in question. In gonorrhœal rheumatism positive results were obtained in a fair percentage of cases by Müller and Oppenheimer(41), Brück(42), and Meakins(43). Positive findings were also reported in typhoid and paratyphoid fevers by Leuchs(36).

Except in its application to the diagnosis of syphilis, where the interpretation of the reaction has already been discussed, the original view of Bordet and Gengou that the method indicates the union of antigen and antibody has been very generally accepted and it is believed by most investigators that it is an antibody *sui generis* which is concerned here and not the precipitins, agglutinins or bacteriolytic amboceptors.

PRECIPITIN TEST.

The value of the precipitin test has been so thoroughly established by the work of Nuttall, Wassermann, Uhlenhuth and many others, that it is unnecessary to review the literature upon this subject. However, there are a few recent works that may be mentioned briefly.

Carnwath(45) has of late described a modification of the technique by which he is enabled to obtain a positive result with very minute amounts of material. The essentials are that the minute blood stain is dissolved in a very small amount of salt solution; that very small glass tubes about 2 millimeters in diameter and 6 millimeters long are employed for the test; that the specific antiserum is introduced by means of a capillary pipette and upon this the suspected fluid is carefully placed in a separate layer. A positive reaction is shown in a few seconds at the zone of contact of the two fluids as a cloud, which gradually spreads upward. This method is very delicate and enables the observer to secure definite reactions with minute quantities of antiserum and of antigen. Carnwath was also able to apply the Neisser and Sachs method of following the precipitin test with the deflection test with these minute quantities, but he agrees with Uhlenhuth that this is unnecessary.

Uhlenhuth in 1903 concluded that it is better in forensic cases to employ only such an antiserum as would produce a definite clouding within one or two minutes with a 1: 1000 dilution of the suspected material when there is one part of serum to 20 of the dilution.

Michaelis and Dehne(46) find that a specific precipitate is dissolved in the presence of an excess of undiluted homologous antigenetic serum. Dehne finds that this is particularly valuable to supplement the test with very minute quantities of antigen; the homologous serum from the known species being added in case of the positive reaction with the extract of suspected material. He also finds that when a specific antiserum produces clouding with the heterologous serum, the precipitate is dissolved equally well by the addition of homologous or heterologous serum.

Weichardt(46) and Stranon(47) attempt to distinguish between individuals by obtaining a highly immune serum, determining its exact value, dissolving as much as possible of the antibody with the serum to be tested and finally adding serum from the homologous individual to determine how much antibody remains. Loele(48) finds he has satisfactory results with precipitin when the material used for inoculating his rabbits was preserved with two per cent formalin in normal salt solution.

EXPERIMENTAL WORK.

In two cases we were called upon to determine the nature of suspected blood stains upon some clothing of natives accused of murder. In the first case the accused alleged that the stains were chicken blood. There were minute flecks upon the surface of a cheap khaki garment which had not been absorbed into the fiber. The stains were examined about five months after the murder, having been kept meanwhile in a safe at room temperature. Extracts made with distilled water and subsequent addition of 1.7 per cent salt solution were colorless, the sediment having a dark, brown color. The hæmin test, precipitin and fixation tests were all negative, and we concluded that the stains were not due to blood. The fixation and precipitin tests were conducted both with antihuman and antichicken serum.

In the second case there was a stain on a cheap cotton garment, which measured about 1.5 by 1 centimeter. The stain had penetrated the fiber and gave an extract which was positive for hæmin crystals, and which gave excellent precipitin and fixation reactions with antihuman serum. The accused claimed that the blood was from a carabao, but as neither precipitin nor fixation tests could be obtained by using anticarabao serum with the stain, we made a diagnosis of human blood.

In this latter case the precipitin test was eminently satisfactory and gave an excellent ring of precipitate in varying dilutions of the extract. The fixation test also yielded excellent results.

Since in the Philippine Islands and particularly in Manila four races of men, Malay, Mongolian, Caucasian and Negro are represented, it would be of no small importance medico-legally, if we could distinguish between these bloods by means of biologic tests. Bruck(16) had already claimed that this could be done by means of the deflection method, before we undertook these experiments to determine whether either the deflection method or precipitin test furnished sufficiently reliable results for this purpose.

At the same time a comparison of the two methods was made in the differentiation of the blood of the various species of cows to be found in Manila.

A number of rabbits were immunized, some against Caucasian blood, others against Filipino, monkey (*Cynomolgus philippinensis* Geoff.), chicken, and carabao serums. Of the antiserums obtained, one anticarabao serum gave precipitation with normal salt and with all mammalian serums, though not with chicken and duck serum; another serum, an anti-Malay (Filipino) serum, gave some reaction with the serum of a rat; otherwise all of the antiserums were specific as is shown in the following table:

TABLE VII.—*Precipitin reactions.*

Dilution of serum from—	Serum of anti-Caucasian rabbit No. 3168.	Serum of anti-Filipino rabbit No. 3167.	Serum of anti-monkey rabbit No. 3195.	Serum of anticarabao rabbit No. 3008.	Serum of anti-chicken rabbit No. 1214.
Caucasian	+	+	+	+	0
Filipino	+	+	+	+	0
Monkey	+	+	+	+	0
Carabao	0	0	0	+	0
Chicken	0	0	0	0	+
Duck	0	0	0	0	+
Dog	0	0	0	+	0
Cat	0	0	0	+	0
Rat	0	+	0	+	0

Pieces of filter paper were moistened with a drop or two each of various serums and were allowed to dry and remain at room temperature for from one to three months. They were then extracted with distilled water and an equal volume of 1.7 per cent salt solution was added to each preparation. These extracts were tested against each of the varieties of precipitin serum and it proved easy to differentiate the albumens in this way. By using an anti-Caucasian and antimonkey serum with varying dilutions of the extracts it was not difficult to distinguish even between monkey and human serum.

The precipitin technique used throughout the experiments was the ring method. A drop of undiluted antiserum was placed in a small tube of from 3 millimeters to 6 millimeters in diameter; upon this a dilution of test material was placed with care to preserve the line of contact between the two fluids. A precipitin reaction became evident very quickly in a ring of precipitum at the junction of the two fluids, exactly resembling the albumen ring in the nitric acid test for albuminous urine. It was found that most accurate readings could be made in from 15 minutes to about one hour, the reaction being less distinct after mixing of the two fluids occurs.

The technique of the deflection method has already been discussed at length.

A specimen of Caucasian blood was obtained from an American and specimens of blood were also obtained from a Negro, Chinese, Japanese, Negrito, Tagalog and monkey. Dilutions of these serums were prepared and simultaneous tests were conducted by the precipitin and fixation methods. The results were as follows:

Precipitin limits of anti-Caucasian serum No. 3332.

Monkey 1 to 1,000.
Negrito 1 to 1,000.
Tagalog 1 to 2,000.
Negro[8] 1 to 800.
Chinese 1 to 2,000.
Caucasian 1 to 3,000.
Japanese 1 to 3,000.

Precipitin limits of anti-Filipino serum No. 3167.

Tagalog 1 to 2,400.
Chinese 1 to 2,400.
Japanese 1 to 2,400.
Negro 1 to 1,800.
Negrito 1 to 1,800.
Caucasian 1 to 1,200.
Monkey 1 to 1,000.

The limits here recorded indicate the greatest dilution of the serum which still gave a trace of reaction with the antiserums and, as it is extremely difficult to determine with certainty the exact position of these limits, it seems to us that the differences obtained can have but little, if any, practical value. However, the anti-Caucasian serum does precipitate Chinese, Japanese, Tagalog, and Caucasian serums at greater dilutions than it does monkey, Negro, and Negrito and likewise the anti-Filipino serum gives precipitation with greater dilutions of Filipino, Chinese, and Japanese serums than with those of the Negro, Negrito, Caucasian, and monkey. This last finding is especially interesting because it is directly contradictory to the rather remarkable conclusion arrived at by Bruck(16) from his deflection experiments. He found that anti-Caucasian serum gave deflection with Caucasian serum 1 to 1,000, Arabian 1 to 900, Chinese 1 to 700, Malay 1 to 500; that anti-Chinese serum showed the same limits with Chinese and Caucasian serums, but required more of the Malay serum; that with anti-Malay serum the same limits were obtained for all three serums. He therefore concludes that the protein of the Caucasian contains all the groups of the Chinese and Malay proteins and in addition certain groups peculiar to itself; that the protein of the Chinese contains all the groups of the Malay and certain other groups not contained in the Malay protein.

In deflection of complement tests conducted with dilutions as close together (600, 700, 800) as is indicated in Bruck's tables, the difference in the degree of hæmolysis in the adjacent tubes is so slight that it becomes very difficult to say where the limit of deflection lies and we believe that Bruck's tables indicating a sharp dividing line between the blocking of hæmolysis and hæmolysis are misleading, although we recognize the fact that in all probability his results were so tabulated simply for the sake of clearness in presentation. It would appear to us, therefore, that Bruck was not justified in assuming such a fundamental difference in the biological reaction on the basis of such slight experimental differences, and we are confirmed in this opinion by the fact that our precipitin experiments indicate that the established laws of the biological reaction hold also for very closely related serums. In our hands the deflection test with anti-Caucasian and anti-Filipino serum showed differences between monkey and Negro on the one hand and Caucasian, Filipino, Japanese, and Chinese on the other, although we could not distinguish with certainty between Filipino, Caucasian, and Chinese as Bruck claimed he was able to do. Hence we conclude that neither the deflection of complement method nor the precipitin reaction can be used with safety in medico-legal cases to distinguish between the bloods of different races of men.

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[8] As the Negro serum was cloudy, it was subjected to repeated centrifugation during the course of these tests and a not appreciable amount of proteid matter was thus removed, so that the dilution was probably really greater than 1 to 800.

A further comparison of the two methods was made with the serum of rabbits immunized to carabao serum, and the results are recorded below:

Precipitin limits with anticarabao serum (average of three determinations).

Carabao, 1 to 3,000.
Chinese cow, 1 to 900.
Native cow, 1 to 900.
American cow, 1 to 650.
Goat, 1 to 150.

The precipitin tests indicate that the native Filipino and Chinese cow are equally removed from the carabao, the American cow being further removed than either of these. The deflection tests gave less clearly defined results than the precipitin reaction and showed the American and Chinese cows to be about equally removed from the carabao, the native being still further removed. It has been shown repeatedly that the antibody concerned in the deflection of complement is not identical with the precipitins, but nevertheless the lack of agreement in the instance cited is rather striking and indicates that the real nature of the deflection reaction has not yet been fathomed.

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TUBERCULO-TOXOIDIN AND IMMUNIZATION SERUM.[1]

By T. Ishigami.[2]

One of the great misfortunes of mankind is that as yet there is no perfect scientific method of successfully combating man's stubborn enemy, tuberculosis. In my belief, the only rational and promising cure for this disease in modern thereapy is the bacteriologic one.

As Koch's preparations prove efficacious on incipient tuberculous patients in many instances only when administered with a careful avoidance of the reaction, the first and most natural step to be taken in our study of the cure is one toward methods of obviating the reaction. After continuous investigations for more than ten years, I have succeeded in preparing two remedial agents of comparatively great efficacy and free from any detrimental reaction.

(1) The first is a chemical preparation from tubercle bacilli and is applicable to incipient and feverless patients.

(2) The other is an immune serum and is applicable chiefly to patients in an advanced stage of the disease.

I introduced these in the belief, based on my own experience of several years, that they were harmless and effective, although not absolutely infallible remedies for tuberculosis. I have since received the corroboration of many practitioners who recognize their efficacy and harmlessness. In this paper I will attempt to describe them briefly.

TUBERCULO-TOXOIDIN.

This preparation is made by chemically dissolving the tubercle bacilli and modifying their toxic property, thus eliminating the reaction which is the common detriment of all other preparations made from tubercle bacilli.

According to the modern theory of immunization, a strong immunity can not be attained without employing strong toxin. Therefore, the question will naturally suggest itself as to whether immunization can be imparted by employing a chemically transformed and harmless toxin. My honored masters, Professors Kitasato and Behring, succeeded in achieving their epoch-making discovery of the serum therapy of tetanus and diphtheria by first attenuating the virus by means of chemical reagents and then immunizing animals with it. Ehrlich's tetanus-toxoid, which is obtained by chemically treating the virulent toxin until it is harmless to animals, still retains the power to immunize them and to neutralize the anti-toxin.

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[1] Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, Manila, P. I., February 28, 1908.

[2] Director of the Ishigami Institute for Infectious Diseases, Osaka, Japan.

Considering these facts, it is quite a natural step to apply the same principle to the subject of tuberculosis and to expect a successful solution of the problem. From my own experience of many years, I find that for the purpose of curing tuberculosis, bacterial immunization is necessary and that, as the absorption of the tubercle bacilli from the subcutaneous tissue of man and animals is extremely difficult, they must first be chemically dissolved and thus made absorbable.

METHODS OF PREPARING TUBERCULO-TOXOIDIN.

The culture of the tubercle bacilli is well soaked and washed with water to remove the soluble toxin. It is then thoroughly dried and weighed, and, after washing again with water, it is treated with strong sulphuric acid in order to disintegrate the bacterial body and thus extract the inner-toxin and change its toxicity. Then, after adding a large amount of water, stirring and allowing to stand for some time, the fats and aromatic oil rise to the surface, leaving the active substance in the bottom in the form of a precipitate. This precipitate is gathered on a filter paper and well washed with distilled water until it becomes neutral. Five-tenths gram of the dried product is dissolved in 100 cubic centimeters of a solution of weak alkali to form a brown, clear liquid.

Although the preparation of tuberculo-toxoidin is such a simple matter, the duration of soaking in the sulphuric acid must be carefully regulated according to the virulence of the bacilli; otherwise the toxicity may still remain too great, or the whole may be rendered useless by carbonization. Therefore, more or less skill in manipulation is required in preparing the toxoidin.

This substance when injected subcutaneously in man or animals is easily absorbed without local irritation, and, as the toxic property is already changed, comparatively large doses can be injected without harm; yet while it is harmless, it is as effective in immunizing man and animals as Ehrlich's so-called tetanus-toxoid. Hence the name "tuberculo-toxoidin."

The following experiments on animals demonstrate the efficacy and harmlessness of the preparation:

(1) *Test of toxicity.*—No reaction was obtained by the injection of 10.0 cubic centimeters of the tuberculo-toxoidin into the peritoneal cavity of a tuberculous guinea pig, which would have succumbed in twenty-four hours to an injection of 0.1 cubic centimeter of Koch's old tuberculin.

(2) *Prophylactic test.*—Guinea pigs injected subcutaneously with 1.0 cubic centimeter of the toxoidin are generally found to be immune against the inoculation of tubercle bacilli from the fourth until the fourteenth day after the operation.

(3) *Therapeutic experiments.*—If the treatment of a guinea pig subcutaneously inoculated with tubercle bacilli commences within one week of the inoculation, and 0.5 to 1.0 cubic centimeter of the toxoidin is injected subcutaneously about ten times, the disease will either be cured or prevented from making further progress. If, two or three weeks after the inoculation of bacilli, the injection of the above doses is made into an animal with greatly swollen glands, the swelling subsides, the body weight increases, and the fatal period is postponed; whereas a control animal dies in three months, the test animal receiving injection treatment lives over a year. When such an animal is killed, autopsy demonstrates that the tuberculous lesions of the organs are not entirely healed. This is due to the fact that guinea pigs are too susceptible to tubercle bacilli to allow of a complete cure.

A noteworthy fact is that in the guinea pigs treated with the toxoidin, the visceral tubercles generally show a tendency to heal and the number of cells containing bacilli is much greater than in those which have not been thus treated. Moreover, the bacilli in the cells are small and short, evidently representing a degenerate form.

CLINICAL APPLICATION.

From my own experience and the reports of other practitioners who have tried the preparation, the following conclusions may be drawn:

(1) By injecting the preparation in a gradually increasing dose into tuberculous patients without fever, almost every one of them increases in body weight and vital capacity, and becomes conscious of the alleviation of the symptoms.

(2) The bacilli in the sputum are gradually broken up and agglutinated and finally disappear, although in some rare cases small amount of expectoration containing bacilli are found for a long time.

(3) The quantity of opsonin in the patients' blood is found gradually to increase by the injection treatment.

(4) The incipient and feverless tuberculous patients, almost without exception, can be completely cured from within three to six months by injection of this preparation.

(5) In patients in a more or less advanced stage, if nutrition is good, similar results can be obtained. In feverish patients, a satisfactory result is often obtained by means of the injection used side by side with antipyretics. In more serious cases, beyond a certain degree, the treatment is quite useless.

(6) Those patients who are once cured or alleviated by this treatment only very seldom suffer from a second attack.

(7) Out of a total of 772 tuberculous patients, each of whom had received more than fifteen injections of tuberculo-toxoidin in my clinic within the past few years, there were 274 who were completely cured and 258 who were partially cured. These last two figures added together make 532, being 68.91 per cent of the total number of patients. Those who for various reasons discontinued the treatment numbered 107; those who died numbered 29; the remainder, 104.

(8) Out of a total of 778 patients treated with the tuberculo-toxoidin (injected

more than fifteen times) by other practitioners, there were 232 who were completely cured and 228 who were partially cured. These last two figures combined make 460, equal to 59.13 per cent of the total number of patients. Those who discontinued the treatment for various reasons numbered 162; the deaths 63; and the remainder, 93.

IMMUNE SERUM.

The results of previous investigators on the problem of the serum therapy of tuberculosis, although undoubtedly very valuable, have not yet reached a stage to permit of the general application of serum therapy to patients. My own investigations of previous years have also failed, because of the difficulty in immunizing animals against tuberculosis and of the characteristic detrimental reaction of the animal serum upon tuberculous patients. I have finally succeeded, however, by means of the injection of the tuberculo-toxoidin, in preparing an immune serum of a comparatively strong efficacy. I have also succeeded in removing the characteristic reaction of animal serum upon tuberculous patients in the manner mentioned below.

When an animal serum is injected subcutaneously into tuberculous patients, there are often noticed characteristic violent reactions such as acute urticaria about the injected area, redness of the face, palpitation of the heart, increased respiration, itching of the entire surface of the skin and, though rarely, pain in the joints. All these symptoms, which disappear in from five to thirty minutes, are doubtless due, as maintained by Dr. S. Ogata, to the agglutination of the red blood corpuscles.

When the serum of a goat, a cow or a horse is treated with from 2 to 3 per cent of sodium chloride, kept at 50° C. for thirty minutes, and then filtered through a Chamberland filter, it can be clearly shown under the microscope to have entirely lost the power of agglutinating the blood of tuberculous patients or of healthy people, and, usually it no longer causes any reaction, either local or general, on injection into a patient.

EXPERIMENTS ON ANIMALS.

When 0.1 cubic centimeter of Koch's old tuberculin, which is the fatal dose to a tuberculous guinea pig, is mixed with 0.025 cubic centimeter of the immune serum, and the mixture after ten minutes' standing is injected subcutaneously into a tuberculous guinea pig, there is not the slightest disturbance noticed in the animal.

When the phagocytic phenomena are examined according to Dr. Wright's method, my immunization serum presents decidedly more marked phagocytic activity than other sera.

When 0.5 cubic centimeter of the immune serum diluted to four times its volume is injected subcutaneously every other day into a tuberculous guinea pig with markedly swollen lymphatic glands, the swelling of the glands is greatly reduced after about ten injections. By further continuing this treatment, the course of the disease is arrested in spite of the fact that the tuberculous lesions of the organs are not yet completed healed. The microscopic sections show the bacilli engulfed in the cells becoming smaller and smaller, thus indicating the degeneration produced by the serum.

CLINICAL APPLICATION.

Generally speaking, as has already been stated above, my immune serum does not when injected subcutaneously cause any local or general reaction; still, in some exceptional cases of idiosyncrasy, a reaction may be noticed. When, however, the immune serum is administered internally as described elsewhere, it produces nearly the same results as by subcutaneous injection, but without any reaction. Hence, except for cases demanding quick or local results, it will be found safer and more convenient to administer it internally.

The following cases require subcutaneous injection:

(1) The cases of acute tubercular cerebral meningitis in which the exudation is not yet marked.

I have three records of satisfactory cures attained by injecting the serum into children who had fallen into stupor from tubercular cerebral meningitis. I have also several records of much alleviation by the serum injection of cases of cerebral meningitis appearing in the course of pulmonary tuberculosis.

(2) The cases of tubercular peritonitis having painful indurations.

(3) The cases of painful tubercular arthritis.

In the following instances, either the injection or the internal administration is employed, as the circumstances demand:

In cases of pulmonary tuberculosis with high fever or with disordered nutrition, when the patients are unfit for the tuberculo-toxoidin treatment, the serum injection is first to be resorted to. When the symptoms are alleviated and the fever disappears and nutrition is restored, the tuberculo-toxoidin is injected in the usual manner.

According to the results of the serum treatment performed in my sanatarium, out of a total of 189 patients, 43 were completely cured and 63 partially cured. These last two figures added together give 106, being 56.08 per cent of the total number of patients. Those who, for various reasons, discontinued the treatment, numbered 37; those who died, 24; and the remainder, 22.

(1) The average number of injections for those who were completely or partially cured was 55 per capita.

(2) The increase and decrease of opsonins were greater during this treatment than in the tuberculo-toxoidin treatment.

(3) The body weight and vital capacity generally increase as a result of the serum treatment.

(4) The phenomena of agglutination, degeneration, and diminution of the bacilli are similar to those of patients under the toxoidin treatment.

Judging from the percentage results summarized in the figures above, the result of the serum treatment appears to be somewhat inferior to that obtained with tuberculo-toxoidin. As, however, the serum is employed generally in the more serious cases, while the tuberculo-toxoidin usually is injected in less advanced cases, the above figures are not strictly comparable with each other. If the advanced patients are first treated with the serum until the symptoms are alleviated and are then injected with tuberculo-toxoidin, a much better result is obtained.

INTERNAL ADMINISTRATION OF TUBERCULO-TOXOIDIN AND IMMUNE SERUM.

The subcutaneous injection of the tuberculo-toxoidin is, as stated above, the safest and most efficacious of all modern therapeutic methods for the alleviation of tuberculosis. However, as this form of injection always requires proper precautions, there are many patients who are prevented thereby from receiving the treatment. Moreover, sometimes, though rarely, there are encountered patients of constitutional idiosyncrasy in whom the injection of the serum causes a reaction. For such cases we are necessarily obliged to resort to a simpler method of administering these cures.

I have ascertained by experiments on animals that the internal administration of the tuberculo-toxoidin and immune serum is harmless and efficacious. Consequently, I have tried the same method on patients for the past few years and found it comparatively efficacious and free from any reaction.

It is difficult to obtain results by administering the tuberculo-toxoidin and the immune serum in liquid form. If administered in the form of pills, however, they are partially absorbed without change, as is seen from the following facts:

(1) Those patients in whom the injection of tuberculo-toxoidin causes fever are also subject to the rise of temperature by the internal administration of the toxoidin pills in comparatively large doses.

(2) Those patients in whom urticaria is produced by the injection of the serum also develop the same symptoms on administration of the serum pills in comparatively large doses.

When patients in an advanced stage receive the toxoidin injection, I administer the pills at the same time in the following manner:

The serum pills are given first until all the symptoms are sufficiently alleviated. The toxoidin pills are then substituted and, in the meantime, the number of injections is gradually diminished. The administration of the pills is maintained for a long time after stopping the injections in order to prevent the diminution of the immunity attained. This particular method of treatment has proved itself to be most effectual.

In the liquid state, the efficacy of the tuberculo-toxoidin and of the immune serum is uncertain, probably because of changes due to the action of the gastric juice. In the form of pills they seen partially to escape the action of the digestive juices and to be absorbed from the intestinal wall.

A NEW INTESTINAL TREMATODE OF MAN.

(FASCIOLETTA ILOCANA, gen. nov., sp. nov.)

By PHILIP E. GARRISON.[1]
(*From the Biological Laboratory; Bureau of Science, Manila, P. I.*)

In April, 1907, during routine examination of fæces, at Bilibid Prison, Manila, P. I., an ovum was found about 100 microns long, oval in form with one end more sharply rounded; shell, light brown in color and of medium thickness, with an operculum at the sharper end; contents rather refractile, colorless, and composed of a mass of yolk-cells, among which the germ-cell could in some cases be distinguished.

In May, and again in September of the same year, eggs of the same description were found in the fæces of two other natives prisoners and in April of the present year still two other prisoners showed the same ovum.

One of the first three patients was discharged without treatment, two were treated for other parasites and the stools examined for the worms which were the source of the eggs in question, none being found.

The two cases of April of the present year (prisoners Nos. 6667-D and 6612-D) arrived at the prison during the same week. The first was treated for a rather heavy infection with *Ascaris lumbricoides*. Several of these parasites were passed, but no other worms were found, although upon subsequent examinations the undetermined ova had disappeared from the stools.

Treatment with male-fern was advised in the case of prisoner No. 6612-D upon the supposition that we might be dealing with an intestinal trematode[2] and this treatment was administered by Dr. E. C. Shattuck, resident physician of the prison. The stools passed after treatment were examined by my student assistants, Mr. Ricardo Leynes and Mr. Rosendo

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[1] Assistant surgeon, United States Navy; detailed medical zoölogist to the Biological Laboratory, Bureau of Science, Manila, P. I.

[2] The use of male-fern in infections with intestinal trematodes was first suggested to us by Dr. Ch. Wardell Stiles in his lectures at The United States Naval Medical School, upon the theoretical ground that a drug which is effective for cestodes might be also for other plathelminthic parasites.

Llamas, of the Philippine Medical School, who found 21 small trematode worms.

Superficial examination of the parasites showed that they were *Fasciolidæ,* but did not belong to any species reported for man, and after study of stained specimens I was unable to ascribe them to any recognized genus of this family. On May 4, 1908, a preliminary report of the parasite was made before the regular monthly meeting of the Manila Medical Society, giving a brief description, but without definitely determining the systematic position of the worms.[3]

The further study of stained and sectioned specimens has furnished the data for the following more complete description.

DESCRIPTION OF TYPE SPECIMENS.

In addition to the diminutive size of the parasites, they are remarkable for the size and prominence of the ventral acetabulum and for the general contour of the body, which is broadest in the region of the acetabulum and tapers posteriorly throughout fully two-thirds its length. In its anterior third, the body appears almost round, but becomes increasingly flattened dorso-ventrally toward the caudal end. A cephalic cone is absent, but the extreme anterior portion of the body (about one-eighth) is more or less distinctly marked off from the remainder by the prominence of the acetabulum itself and the rapid lessening of the transverse and dorso-ventral diameters anterior to the acetabulum, and also by a more or less distinct transverse depression in the ventral surface slightly anterior to the acetabulum. The anterior portion thus marked off appears in some specimens almost like a cephalic appendage, an appearance which is heightened by the fact that after preservation this anterior part of the worm is frequently bent sharply dorsad out of line with the longitudinal axis of the remainder of the body.

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[3] The following extract is taken from the proceedings of the monthly meeting of the Manila Medical Society of May 4, 1908:

"Doctor P. E. Garrison.—*A new trematode parasite of man.*

"Author's abstract.—Ova found five times in native prisoners at Bilibid during the past year; 21 worms obtained from last case after dose of male-fern. Patient complained of no symptoms; physical examination negative, except a slight anæmia. Hookworms and whipworms also present. *Morphology of parasites:* Small *Trematoda,* of the family *Fasciolidæ*; 4, 5 to 6 millimeters long by about 1 millimeter broad; broadest at junction of anterior and median thirds; skin without spines; acetabulum near and much larger than oral sucker; pharynx globular; œsophagus very short; intestinal caeca unbranched and extend to posterior extremity; male and female genital pores open separately between acetabulum and oral sucker, slightly to left of median line; testicles posterior, median, one directly behind the other, each divided into anterior and posterior lobe by median transverse constriction; ovary anterior to testicles; shell gland between testicles and ovary; uterus moderately developed; vitellogene glands highly developed, extending from plane midway between acetabulum and ovary to posterior extremity, meeting in median line ventrally and encroaching upon median field dorsally after they pass caudad of the testicles; posterior excretory tract divides just behind testicles into two lateral excretory canals. Ova average 107 μ long by 63 μ broad, with prominent operculum at one end, unsegmented at oviposition, develop ciliated embryo, which hatches in about one week. Specific and generic position of parasite not yet difinitely determined, the indications being that it may be necessary to create a new species and perhaps a new genus also. (Specimens and photographs demonstrated.)"

The posterior extremity (about one-fifth) of the body also is more or less distinctly differentiated from the remainder by a slight, but rather abrupt shortening of both the transverse and dorso-ventral diameters and also by its darker color, due to the extension of the vitellaria across the median field in this portion of the worm.

The remaining, middle portion of the body, comprising something over three-fifths of its length, contains anteriorly the large and prominent ventral acetabulum, behind which this portion of the body is more or less distinctly marked off into five longitudinal tracts or fields, namely, two lateral fields along each lateral margin, containing the intestinal cæca and the vitellaria, a median field containing anteriorly the coils of the uterus, and posteriorly, the ovary, shell-gland and testicles, and two light colored sub-lateral fields separating the median from the two lateral fields and marking the course of the two main branches of the excretory tracts.

Dimensions.—Fifteen specimens gave the following measurements in millimeters:

Length.	Maximum breadth.	Maximum thickness.
4.25	1.00	0.70
4.00	0.80	0.60
4.50	1.00	0.70
5.50	1.25	0.80
5.00	1.00	0.75
5.00	1.20	0.80
4.00	0.75	0.50
4.25	1.00	0.70
5.00	1.00	0.80
6.00	1.35	1.00
5.25	1.00	0.80
4.00	1.00	0.60
4.50	0.80	0.60
5.80	1.00	0.70
4.00	0.75	0.50

Maximum, 6 millimeters long, 1.35 millimeters broad, 1 millimeter thick; minimum, 4 millimeters long, 0.75 millimeter broad, 0.50 millimeter thick; average, 4.74+ millimeters long, 0.99+ millimeter broad, 0.70 millimeter thick.

Cuticle is smooth and without spines.

Pigmentation is slight and evenly distributed; the fresh specimens were of a semi-transparent red-gray color and the testicles, ovary, vitellaria and uterus were distinctly visible under a hand lens.

Ventral acetabulum.—The acetabulum measures from 480 to 520 μ in diameter (about half the maximum transverse diameter of the body) and is situated with its center at just about the junction of the first and second anterior fifths of the body.

Alimentary tracts.—The *oral sucker* is terminal or slightly ventro-subterminal, the greater development of its dorsal side giving the oral opening a more or less marked inclination toward the ventral surface. It measures from 130 to 200 μ transversely and dorso-ventrally by from 75 to 130 μ antero-posteriorly (about one-third the size of acetabulum). From the oral sucker to the pharynx extends a short, rather broad *prepharynx* which in some specimens appears almost obliterated by the close approximation of these two organs, while in others it is considerably extended, its length in different specimens varying from 10 to 63 μ. The *pharynx* is globular and measures from 150 to 190 μ in diameter. The *œsophagus* is very short (50 to 100 μ), its bifurcation occurring just anterior to the plane of the genital pores. The thin walled *intestinal cœca* pass rather sharply outward toward the lateral margins and then follow these margins rather closely to near the posterior extremity of the body, one cæcum sometimes reaching a slightly more posterior position than the other. Before they reach the equator of the body the cæca become bounded laterally, and also to some extent ventrally and dorsally, by the vitellogen glands.

Excretory tracts.—In the posterior fifth of the body the excretory tract is single and dilated into a cavity of considerable size with irregular, ill-defined walls ("excretory bladder"). On reaching the posterior border of the caudal testicle the tract divides into two lateral branches which pass cephalad between the median and lateral fields above noted to a position dorsad of the acetabulum where approaching the median line, they are separated by only a thin septum. (In some sections the two tracts appear actually to join anteriorly.)

Male organs.—The *testicles* occupy the posterior part of the median field of the middle portion of the body and lie one immediately and directly behind the other in the median line. They are bounded posteriorly and laterally by the excretory tracts. Each testicle is more or less distinctly divided by a transverse circular constriction into an anterior and posterior lobe. In some specimens, this constriction is very slight and the testicle appears almost oval, while in others it is well marked and there may be even slight indentations at other parts of the surface, marking off four or five poorly defined lobules. From each tetsicle the *vas deferens* passes forward through the lateral (marginal) fields to a position dorsad of the acetabulum where the two enter the posterior end of the cirrus pouch. The *cirrus pouch* measures from 560 to 608 μ in length by from 240 to 280 μ in breadth and is situated dorso-anterior of the acetabulum, with its axis directed forward and ventrad, and also slightly to the left side. Posteriorly it contains a large ***vesicula seminalis*** which receives the *vasa deferentia* and which as seen in different specimens appears to be capable of considerable distention. Within the cirrus pouch the *cirrus* is more or less coiled or looped and provided with a well developed musculature and a glandular envelope (*pars prostatica*). In each of the specimens, the cirrus is extruded through the male genital pore and externally is curved in from one to two spiral turns.

Female organs.—The *ovary* is globular and situated at just about the center of the body length, slightly to the right of the median line. Posterior to the ovary, and filling the space between it and the anterior testicle is a well developed, globular *shell gland.* The *vitellaria* extend anteriorly to or slightly behind the junction of the anterior with the middle third of the body length or to a plane about midway between the proximal borders of the ovary and acetabulum. Passing posteriorly, they conform closely to the lateral margins and extend slightly upon the ventral and dorsal surfaces, so that on cross section they give the form of a crescent, in the convexity of which lie the intestinal cæca. After passing caudad of the testicles the vitellaria quickly spread across the dorsal surface and meet in the median line, at the same time encroaching more gradually upon the ventral surface until, in the extreme posterior portion of the body they meet in the median line ventrally also and completely encircle the body, enclosing the extremities of the cæca and excretory tract. The *transverse vitello-ducts* cross the sub-lateral fields (excretory tracts) at the level of the anterior border of the anterior testicle, almost at right angles to the longitudinal axis of the body and enter the postero-lateral borders of the shell gland. *Laurer's canal* present. *Receptaculum seminis* absent. The coils of the *uterus* are fairly developed, extend on the left side as far back as the shell gland, and fill the median field between the ovary and acetabulum, being bounded laterally and separated from the cæca by the broad excretory tracts. The anterior extremity of the uterus continues into the well developed *vagina* which passes forward dorsad of the acetabulum directed slightly toward the left and opens at the *female genital pore,* separate from and situated just to the left of the male pore, the two pores being about midway between planes passed through the anterior border of the acetabulum and the posterior border of the pharynx respectively and just behind the bifurcating intestinal cæca. The site of the genital pores is marked by the transverse depression in the ventral surface above mentioned as more or less distinctly separating the cephalic extremity from the remainder of the body.

Ova.—The ova are not very numerous. The shell is thin, light brown in color, with an operculum at the smaller end. In the fæces the egg-contents are colorless and composed of a number of ill-defined vitellogen cells among which the ovic cell could, with difficulty, be detected in some eggs. The ova, in fresh fæces, vary considerably in size and also in their relative length and breath, some being shorter and thicker than others. The careful measurement of fifty ova in the fresh stool gave the following results, in microns:

99.9×59.2
96.2×59.2
99.9×74.
103.6×62.9
114.7×55.5
92.5×55.5
99.9×66.6
103.6×62.9
88.8×62.9
107.3×59.2
99.9×55.5
96.2×62.9
96.2×59.2
92.5×62.9
103.6×59.2
103.6×59.2
103.6×62.9
99.9×59.2
96.2×74.0
111.0×62.9
114.7×66.6
99.9×62.9
96.2×59.2
99.9×81.9
92.5×62.9
96.2×59.2
99.9×55.5
96.2×59.2
99.9×59.2
103.6×62.9
99.9×59.2
103.6×62.9
96.2×62.9
92.5×59.2
96.2×62.9
111.0×81.9
99.9×59.2
92.5×59.2
92.5×59.2
92.5×66.6
92.5×66.6
92.5×53.5
103.6×62.9
98.0×59.2
103. ×60.
103. ×62.9
103.6×53.5
107.3×59.2
96.2×57.4
94.3×53.5

Maximum dimensions: Length, 114.7; breadth, 81.9 μ.
Minimum dimensions: Length, 88.8; breadth, 53.5 μ.
Average dimensions: Length, 99.58; breadth, 53.5 μ.[3]

When the stools, were repeatedly sedimented until their fæcal character was destroyed, the ova, in about 10 days, developed ciliated miracidia which, raising the operculum, escaped from the shell and swam free in the water. Attempts were made to infect several varieties of snails and one variety of fish with the free miracidia, but without success.

Upon the basis of the characters above described, it is proposed to establish a new genus and species in the family Fasciolidæ, of which these specimens shall be the type and for which we propose the names *Fasciolctta ilocana.*

FASCIOLETTA gen. nov.

GENERIC DIAGNOSIS.—*Fasciolidæ:* Body small, elongate, broader anteriorly than posteriorly. Acetabulum near and much larger than oral sucker. Intestinal tract with short, broad prepharynx, highly developed pharynx, short œsophagus, and long, unbranched cæca, which pass along lateral margins and extend to near the caudal extremity of worm. Excretory system consists of a posterior median stem which, posterior to the testicles, divides into two laterally placed canals which extend anteriorly, separating the testicles, shell gland, ovary and uterus from the cæca and vitellaria. Genital pores anterior to acetabulum. *Male organs:* Testicles massive and compact situated one directly behind the other, in the median line, in posterior portion of body, both caudad of transverse vitelloduct. Cirrus and cirrus pouch highly developed. *Female organs:* Ovary compact, unbranched, situated slightly to right of median line at about the equator of body. Receptaculum seminis absent. Laurer's canal present. Vitellaria most highly developed, in posterior one-fifth where superficially they spread over the dorsal and ventral surfaces, more or less completely encircling the body. Anterior to the caudal border of the posterior testicle they are confined to the lateral fields, conforming closely to the lateral margins of the body, external to the intestinal cæca, and reach a position considerably cephalad of the ovary.

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[3] Measurements made with Zeiss objective D D (9237), correction collar at 20, micrometer ocular No. 3, tube length 145.

Shell gland well developed, situated between ovary and anterior testicle. Uterus coiled in the space bounded laterally by excretory channels, anteriorly by acetabulum and posteriorly by ovary and shell gland. Ova large, operculated, not very numerous, and develop ciliated miracidium after leaving body of host.

HOST OF TYPE SPECIES.—*Homo sapiens:* Habitat; intestine.

TYPE SPECIES.—*Fascioletta ilocana.*

Fascioletta ilocana sp. nov.

SPECIFIC DIAGNOSIS.—*Fascioletta:* Length, 4 to 6 millimeters; maximum breadth, 0.75 to 1.35 millimeters; maximum thickness, 0.50 to 1 millimeter; greatest breadth and thickness a little posterior to the caudal border of the acetabulum. Posteriorly, the body attenuates gradually throughout two-thirds its length to a rounded caudal extremity; anteriorly, for about one-third its length, to a rather sharper cephalic extremity. In the posterior half the body becomes increasingly flattened toward the caudal end. Oral sucker terminal or slightly ventro-subterminal, small (130 to 200 μ transversely by 75 to 130 μ deep); dorsal lip much larger than ventral, giving the sucker a ventral inclination. Ventral acetabulum about three times as large as oral sucker (nearly globular, 480 to 518 μ in diameter), situated with its center at about the junction of the first and second anterior fifths of the body length. Skin smooth and without spines. Pigmentation slight and evenly distributed. Prepharynx from 10 to 63 μ long. Pharynx globular, from 150 to 190 μ in diameter. Œsophagus short (50 to 100 μ). Intestinal bifurcation immediately anterior of plane passed through genital pore. Intestinal cæca thin-walled; follow rather closely the lateral margins of body to near its posterior end, being partly inclosed by the vitellaria throughout considerably more than the posterior half of their course. Genital pores open upon the surface separately to the left of the median line and slightly posterior of a plane midway between posterior border of pharynx and anterior border of acetabulum. *Male organs:* The cirrus pouch is from 560 to 608 μ long by from 240 to 280 μ broad; situated anterodorsad of the acetabulum, with its longitudinal axis directed antero-ventrally and slightly to the left. Posteriorly it contains a bladder-like vesicula seminalis which receives the vasa deferentia and gives origin to a well developed cirrus which takes a more or less coiled course to the male genital pore through which it may protrude in from one to two spiral turns. Vasa deferentia divergent. The testicles lie one immediately and directly behind the other, occupying the median field just caudad of the transverse vitello-ducts. Each testicle is more or less distinctly divided into an anterior and posterior lobe by a transverse, circular constriction, and other slight indentations of the surface may indicate ill-defined secondary lobules. *Female organs:* Ovary globular, situated at equator of body, slightly to right of median line. Vitellaria highly developed, extending antero-posteriorly from the caudal extremity to a plane midway between proximal borders of ovary and acetabulum. Cephalad of the posterior border of the testicles they lie along the extreme lateral margins, filling the space between margins and cæca and extending somewhat upon the dorsal and ventral surfaces, thus inclosing the cæca dorsally and ventrally between the two superficially placed vitellogen layers. Caudad of the testicles, the vitellaria spread over the dorsal surface and meet in the median line, at the same time gradually encroaching upon the median field ventrally. In the extreme posterior portion of the worm (about one-tenth of its total length) they may meet in the median line ventrally as well as dorsally, thus completely inclosing the caudal extremities of the cæca and excretory tract. At the anterior border of the anterior testicle the transverse vitello-ducts pass inward and slightly forward to the well-developed,

globular shell gland which fills the space between the anterior testicle and the ovary. Uterus fairly well developed; its coils filling the median fields between the excretory tracts from the acetabulum to the ovary on the right side and extending caudad of the ovary on the left to the border of the anterior testicle. Its anterior extremity is continued into a well developed vagina which passes diagonally across the median line dorsad of the acetabulum to reach the female genital pore, which is situated just to the outer side of the male pore.

***Ova* from 88.8 to 114.7 μ long by from 53.5 to 81.9 μ broad, averaging 99.58 by 56.04 μ; develop miracidium in about 10 days after leaving host. Further development unknown.**

HABITAT.—Intestine of man.

TYPE LOCALITY.—ILOCOS SUR, Northern Luzon, Philippine Islands.

TYPE SPECIMEN.—Number 240-A (co-types number 240), Helminthological Collection, Bureau of Science, Manila, P. I.

FREQUENCY, LOCALITY, AND PATHOGENISIS.

Over 5,000 native Filipinos, representing all parts of the Islands, have been examined for intestinal worms during 1907 and the first three months of 1908. That only five infections with *Fascioletta* have been encountered would seem to indicate a very low frequency with regard to the population of the Islands as a whole.

However, all five of the infected prisoners came from the northwestern provinces of Luzon, and two of them, including the one from whom the worms were obtained, had lived all their lives in the Province of Ilocos Sur. Accordingly, there is some indication that the parasite may not be equally distributed throughout the Islands.

Only the two cases which appeared in April of the present year were examined clinically. Questions and answers had to be passed through two interpreters (Tagalog and Ilocano) and only fragmentary and rather uncertain information could be secured. Both prisoners had lived in Ilocos Sur all their lives. They had worked bare legged in fields overflowed with water; fish was an important part of their diet; they had not suffered from any sickness except "fever"—which facts, excepting possibly the last, would apply to the great majority of the population. At the present time neither complained of any illness nor would either admit having or having had any intestinal trouble. Physical examination was negative with the exception that one of the prisoners was somewhat anæmic, the hæmoglobin registering about 85 per cent. In this case infections with hookworms and whipworms also were present.

ILLUSTRATIONS.

ac. = acetabulum.
cir. = cirrus.
cir. p. = cirrus pouch.
exc. p. = excretory pore.
exc. tr. = excretory tract.
f. g. p. = female genital pore.
g. p. = genital pores.
int. = intestinal cæca.
L. c. = Laurer's canal.
m. = mouth.
m. g. p. = male genital pore.
œs. = œsophagus.
ov. = ovary.
p. = pharynx.
pp. = pre-pharynx.
sg. = shell gland.
t. = testicles.
trs. v.d. = transverse vitelloduct.
ut. = uterus.
va. = vagina.
vd. = vas deferens.
v. g. = vitellogen glands.
v. s. = vesicula seminalis.

(Photographs by Charles Martin, Bureau of Science.)

PLATE I.

FIG. 1. Photograph. A group of eight specimens of *Fascioletta ilocana*, natural size.

2. Photomicrograph of type specimen from ventral surface. Stained with carmine and picric acid. Enlargement about 18.

3. Semi-diagrammatic drawing showing anatomy.

4. Photomicrograph of longitudinal section in median line. Stained with carmine and picric acid. Enlargement about 20.

5. Semi-diagrammatic drawing showing apparent structure and relations of cirrus and cirrus pouch.

PLATE II.

FIGS. 6, 7, 8, 9. Semi-diagrammatic drawings of transverse sections through (6) cirrus pouch just caudad of genital pores; (7) ovary; (8) posterior testicle; (9) plane midway between testicle and caudal extremity.

FIG. 10. Photomicrograph of ova of *Facioletta ilocana* and *Trichuris trichiura*.

FIGS. 11, 12, 13. Photomicrographs of ova (11) in fresh fæces; (12) showing developed miracidium; (13) showing operculum lifted after escape of miracidium. Enlargement about 320.

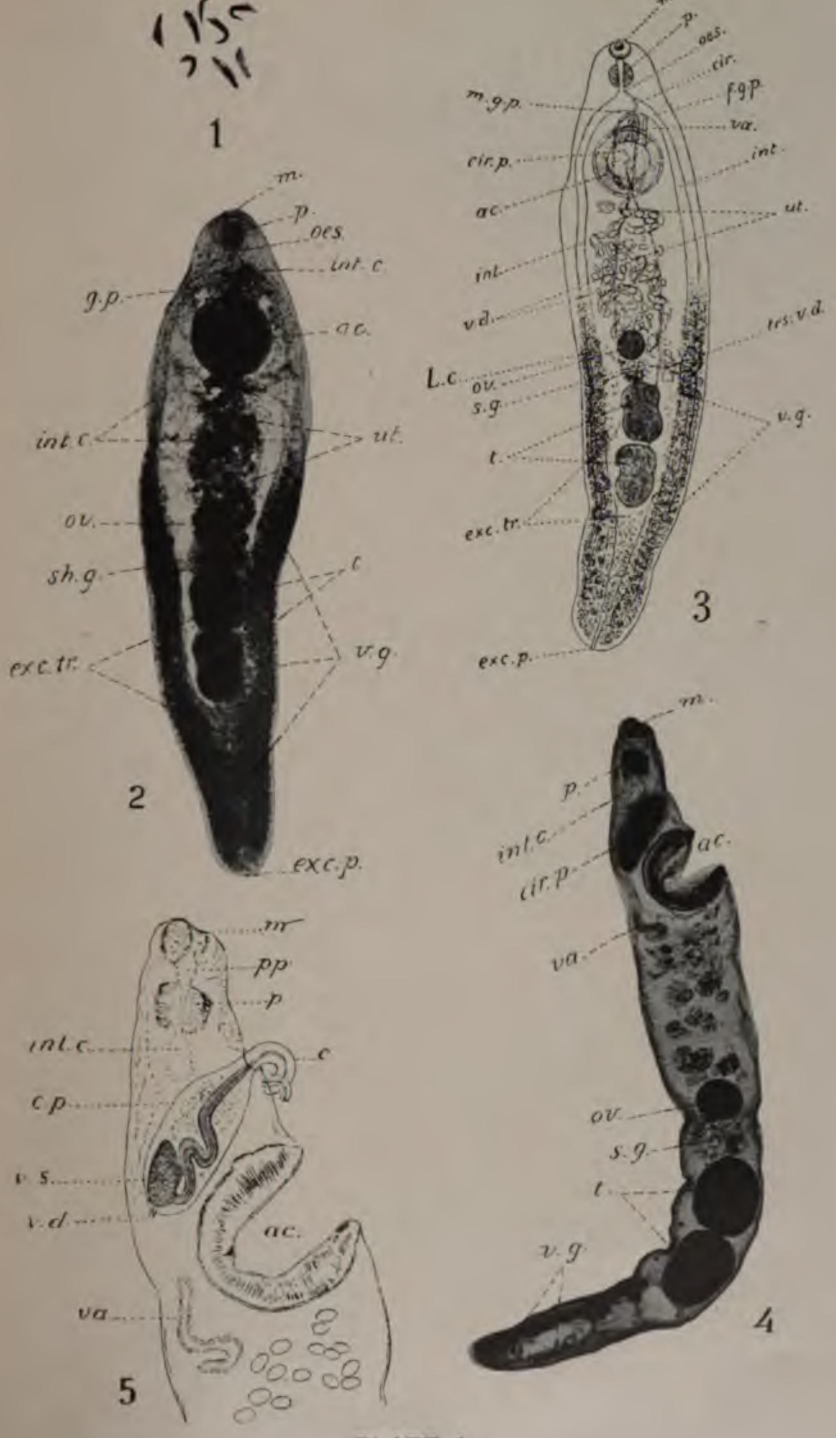
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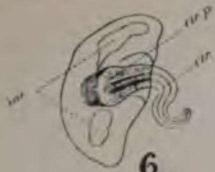
PLATE I.



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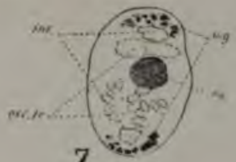

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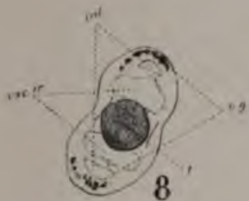

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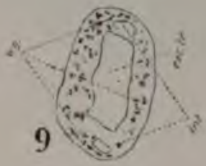

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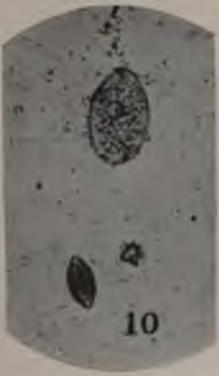

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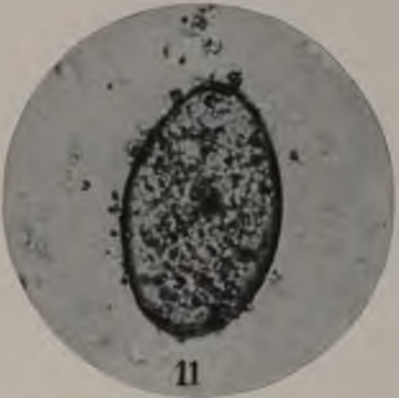

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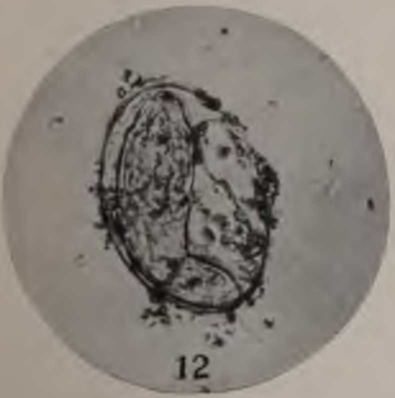

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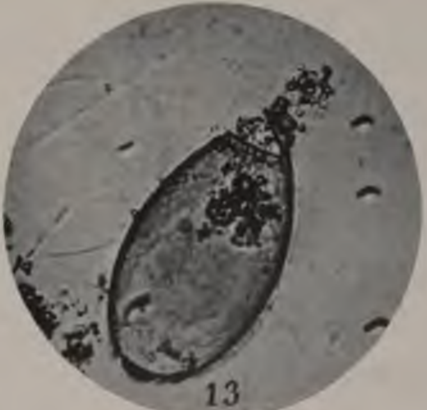

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PLATE II.

BLASTOMYCOSIS OF THE SKIN IN THE PHILIPPINE ISLANDS.[1]

By JAMES M. PHALEN and HENRY J. NICHOLS.[2]

I. INTRODUCTION.
II. PREVALENCE.
III. DIFFERENT FORMS.
IV. ORGANISMS AND CULTURES.
V. OTHER KINDS OF BLASTOMYCOSIS.

I. INTRODUCTION.

Our instructions from the Surgeon-General of the Army state that "parasitic diseases of the skin deserve further study and attempts should be made to isolate and cultivate the fungi causing them." Blastomycosis we have found to be a particularly suitable subject for such a study because of its prevalence and lack of recognition. Blastomycotic infection of the skin was first described in 1894 by Gilchrist and generalized blastomycosis by Busse in the same year. Since then a considerable literature has been produced, in large part by American authors, as is shown by reviews by Hyde and Montgomery, Hektoen and others. The term blastomycosis is a general one and is used here for convenience to designate pathologic conditions produced by double contoured, budding bodies. The botanical relations of these forms to yeasts and fungi, their relations to each other and to such bodies as those of coccidioidal granuloma have not been sufficiently worked out to permit of exact classification. Accordingly, we shall simply call attention to the clinical peculiarities of the disease as we have seen it, to the nature of the organisms and of the cultures obtained and to the presence here of other forms of blastomycosis.

II. PREVALENCE.

We believe that cutaneous blastomycosis is one of the common parasitic skin diseases among both natives and white men in the Philippine Islands. The dispensary clinic of the University Hospital, in Manila, is a rich field for observing these cases among natives. Through the kindness of Doctors Saleeby and Winsor we have been able to study a number of patients at the Dispensary and usually have been able to find without previous arrangement one or more cases. The physicians in charge say that at least one new case of this form of disease applies for treatment each week. Among 50 natives examined on one morning we found 5 cases. In the last eight months we have seen 7 officers with various degrees of the disease and have ceased to keep track of the exact number of enlisted men affected. The infection has been seen in Mindanao, Jolo, Cebu, Panay, Samar, and Luzon, and there is every reason to believe it to be widespread throughout the group of Islands. This is somewhat surprising because among skin diseases common in the Tropics, no mention is made of this condition by Manson, Scheube, Mense, Macleod in Albutt's System or Jackson, nor is the term found in special articles on the skin diseases of different tropical countries. The only account of this form of infection in the Tropics, which we have found, is by Ashburn and Craig. They had a white patient, age 40, with five lesions of two years' duration on his face, resembling ring-worm. Scrapings stained by the modified Gram method showed round, double-contoured bodies lying in and between the epithelial cells. The patient stated that the disease was common among natives, but rare among whites. He improved under potassium iodide internally. No cultures were obtained. There are several references to blastomycotic ulcerations in the East by Sakurane and Okugawa, Japan, 1905; Lukis, India, 1907; Strong, Philippine Islands, 1906, and Shattuck, Philippine Islands, 1907, but the lesions described seem to be different from those with which we are now concerned.

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[1] Read by abstract at the Fifth Annual Meeting of the Philippine Islands Medical Association, Manila, P. I., February 27, 1908.

[2] Captain, Medical Corps, United States Army, and first lieutenant, Medical Corps, United States Army, constituting the United States Army Board for the Study of Tropical Diseases, as they occur in the Philippine Islands.

III. DIFFERENT FORMS.

Clinically the disease appears in three distinct forms, although there are intermediate types from the mildest to the most severe.

A. The mild cases somewhat resemble the commonly observed skin infections with ordinary fungi. The lesions are elevated little, if at all, above the surrounding skin, are irregular in outline, and the surface when freed from scales presents a smooth, reddish surface. The lesions itch considerably, but otherwise give no discomfort. The couse is toward a progressive extension of the patches, with marked induration of the affected skin. The tendency to appear in unusual locations, and the frequency of a symmetrical distribution are the features which distinguish it clinically from ring-worm, with which it has many features in common. It has been observed to occur on the back of the hands, the forearm, shoulder, face, front of the leg, and the toes.

CASE I.—In fig. 1 is given an illustration of a lesion of this class. This patient, a sergeant of an Infantry regiment, first came to the Philippine Islands in 1904 and went to Camp Jossman, Island of Guimaras, for station. In the spring of 1905, while cutting a clump of bamboo at that post, he scratched his right wrist on a thorn. The cut bled a little and he sucked it. A little later the spot became reddened, and itched greatly, and it gradually spread around the wrist. A similar spot appeared upon the palm of his right hand. These spots were treated with various antiseptic ointments and lotions for nearly two years, without much effect until, while at Mount Gretna encampment in 1906, they were healed by the application of a strong alcoholic solution of mercuric chloride. Shortly after, small spots of a similar character appeared upon the left wrist and left leg, and these have persisted and have continued to spread ever since, more rapidly since his return to the Philippines in July, 1907.

He came to us in March 1908, somewhat anxious about his condition as he had been told by a Spanish physician that the disease was likely to affect his internal organs. The lesions present at that time were situated on the outer side of the left leg near the knee and on the back of the left wrist. There were several areas, each 5 to 8 centimeters in diameter, irregular in outline, slightly raised, with a well-defined edge and covered with scales which, when removed, left a pink, glistening surface.

The surface feels rough and indurated. No crusts nor exudate are present. The scales, when removed, treated with a potassium hydrate solution and examined under a high-power lens, show in abundance the organisms illustrated in figs. 6 and 7, a more detailed description of which will be given later. Attempts to cultivate the organism from this group of cases proved unsuccessful. A picture of a section of the skin is shown in fig. 8.

From a study of the sections, the process appears to be twofold. On the one hand there is an overgrowth and widening of the papillary layers. The papillæ show a definite downward growth and often include a small island of connective tissue which appears somewhat like a miliary abscess, but contains no polynuclear cells. On the other hand, the corium in places infiltrates the epithelium, producing a fibrosis and degeneration of the epithelium so that as the section is moved across the field, one part will show an excess of epithelial elements and the next a loss with an increase of connective tissue. A marked infiltration with round cells appears in the deeper layers of the corium.

The majority of these cases are of many months', or even of years' standing. The mildest yield to strong local antiseptics, others only to potassium iodide internally. These infections are usually passed over as a variety of "dhobie itch" and even on microscopic examination of the scales often nothing is seen unless the oil immersion lens is used.

B. The second type of the disease is the one most frequently encountered. In these cases the lesions are in quite large areas, sharply circumscribed and considerably elevated above the surrounding, healthy skin. They are frequently observed to have a border raised above the rest of the patch, this ridge being beset with "miliary" abscesses covered with crusts. The remainder of the area has a red, smooth surface covered with scales.

CASE II.—The patient is a Filipino girl, 8 years of age, from the Tondo district of Manila. No history as to the beginning of or the duration of the disease is obtainable. The lesion shown is irregularly circular in outline, about 7.5 centimeters in diameter, situated back of the left axilla. It presents a crescentic ridge 3 to 6 millimeters high and 13 to 20 millimeters wide, with a concavity upward extending along the lower edge and sides of the patch. This ridge has a number of small pustules opening upon its surface, and is covered by a crust made up of the dried discharge. The center and the upper part of the affected area is occupied by indurated tissue, with a smooth surface covered by fine scales. A smaller area, 4 by 5 centimeters, of a similar character occupies the outer side of the right elbow. This area has a ridge along the posterior border, with some superficial erosion. The rest of the lesion is made up of indurated tissue of a like character to the larger lesion. The scales and crusts show a great quantity of blastomycetes.

CASE III.—This patient is an officer in a Scout organization, and presents the following history: In the early part of 1904, while stationed at Camp Connell, Samar, he noticed a small papule near the middle of his left cheek. He considered it of no consequence, and so does not remember much of its early characters, except that it itched considerably. He does not recollect any injury or abrasion of the face previously. From this beginning the present lesion has extended, at first downward, then forward and upward; at first it was quite superficial and the earlier places were healed by the local application of nitrate of silver. As is customary in these cases, the eruption recurred almost immediately and the patient has never been free from it since.

When first seen by us, in April, 1908, there was present on the left cheek a large, crescentic patch extending parallel to the lower jaw, presenting an indurated ridge along the convexity of the patch and induration of a less degree inside.

The whole area is red and shining, except where covered with scales. Along the ridge, a number of more indurated spots exist, lighter in color, which upon opening exude a small drop of white pus. There are some crusts covering small cavities also containing pus. Examination of the scales and pus in this case reveals in large numbers the same organisms found in the others.

CASE IV.—C. C., Chinaman, 40 years old, a shopkeeper in the Santa Cruz district of Manila, seen at St. Luke's Dispensary. No history is obtainable, except that the lesions present are of eight months' duration, came on gradually and were still extending. This patient has a circular patch, 5 centimeters in diameter, over the center of the back of his neck. This patch has a raised, indurated border and a central portion, indurate, but apparently healed, on the level with the rest of the skin. The surface of the raised border is smooth, glossy and of a dark red color. This patient has also a round, elevated spot, 12 millimeters in diameter at each angle of the mouth and on the right side of the lower lip a patch extending laterally from the angle of the mouth to the median line, and reaching downward for about 25 millimeters, the lower border being scalloped and raised in a sharp ridge. The lesions are bright red and glossy. The scales show a large number of organisms which are indistinguishable from those found in the other cases; a culture was obtained from this case, which will be described later.

A number of other cases of this class have been observed (fig. 2). They all give a history of a long, chronic course, and of resistance to treatment. They have been diagnosed as syphilis, leprosy, tuberculosis and other diseases. However, with the exception of tuberculosis, there is little resemblance to these infections. The case of cutaneous blastomycosis, reported by Ashburn and Craig in 1906, belongs to this second class. Both in appearance and in microscopic findings their description coincides with those that we have given.

The histologic picture of type B is intermediate between those of A and C. The papillæ show more marked overgrowth and the upward growth of the connective tissue reaches the surface of the skin and thus accounts for the formation of crusts. There is a greater infiltration in the deeper layers of the corium. The infiltrating cells are almost entirely of connective tissue in various stages of growth, but there are some unusual cells, large and round, which when stained by hematoxylin and eosin, have a deep black nucleus and a rim of pink protoplasm.

C. This form answers clinically quite closely to the descriptions of cases of cutaneous blastomycosis reported from the United States. One well-marked case of this class has been under observation for the past three months, and one other was seen at St. Luke's Dispensary. (Figs. 4 and 5.)

CASE V.—B. C., male Filipino, 34 years old, a resident of Pasay, and a coachman by occupation. He was born in Pasay and has lived there all his life. He has been married for twenty years, had five children, two of whom died of smallpox, two of intestinal trouble and one, 11 years old, is alive and well. Ten years ago he acquired a small venereal sore which healed in a week. He has no further symptoms to indicate that the sore was syphilitic. There is no evidence of tubercular infection. Two years ago a sore appeared on the right buttock, near the anus, on the site, the patient thinks, of an abrasion due to horseback riding. This healed after three months of dispensary treatment. One year ago, it reappeared on the right buttock, since which time it has spread gradually to its present dimensions.

Present condition (fig. 3).—The lesions occupy nearly the whole of the right buttock, and extend several inches over on to the left. They reach downward on to the back and inner side of the right thigh and up into the groin in front on the right side. The greater part of this area is occupied by scar tissue, but the process is still active in a ridge 5 centimeters wide along the left border of the patch, in an oval area 5 by 7.5 centimeters in the median line above, in the extreme right edge, in the lower part of the right side and in the right groin. Over these areas the surface is raised 3 to 6 millimeters above the surface of the skin. In places there is a fine, papilliform growth with deep fissures intervening and in others broad, warty surfaces, dry or covered with large scales. The papilliform elevations are frequently covered by a large, yellow crust, and the intervening fissures contain pus loaded with blastomycetes.

The patient was put on ascending doses of potassium iodide, and within a week the papillæ began to contract and became smoothed over and ceased to secrete an exudate. In two months the disease was apparently entirely cured. although some induration remained. A culture was obtained from this case.

A section (fig. 8) from a lesion of this form shows a great overgrowth of epithelium, which superficially resembles an epithelioma. However, the cells are more regular in size, shape, and arrangment. Pearls are occasionally seen. The increase of connective tissue is also very marked and it reaches the surface in wide processes, showing a great deal of exudation of blood cells. The epithelium in its growth incloses a great many small areas of connective tissue. The hair and sweat glands are apparently not involved in the overgrowth.

Clinically it seems as if the milder forms did not develop into the more severe. This can only be decided by further observation, especially of cultures obtained.

The diagnosis depends on finding blastomycetes in the lesions constantly and in such number that they can not be regarded as accidental. Control examinations of scales, crusts and pus from other lesions have shown occasional blastomycetes, but these are not constantly present nor in such numbers as are seen in the lesions described. Of course, sections and cultures are desirable, but in our experience the latter are difficult to obtain and are unnecessary before starting treatment. After seeing a number of cases we have been able to pick out others from their clinical appearance. In the milder forms the presence of blastomycetes and absence of any fungi in a manifestly parasitic disease differentiate the affection from ring-worm, *Tinea imbricata,* etc. The severe forms may be taken for tuberculosis or syphilis. If tuberculous they will not heal up in one to two months of treatment with potassium iodide. The history and clinical appearance differentiate the affection from syphilis, as in the latter disease there is no such overgrowth of the epithelial structures. In tertiary yaws the lesions are ulcerative, while in this form of blastomycosis of the skin no definite ulcerations have been seen.

IV. ORGANISM AND CULTURES.

We have been unable morphologically to distinguish any difference in the organisms from the various cases. If a scale is taken from type A, or a crust or some pus from either B or C and macerated thoroughly in a ten to twenty per cent solution of potassium hydroxide, the organisms become very distinct. Their most striking feature is a double contour, usually less than 1 μ thick, but occasionally some are seen in which it is 2 μ. There is a great variety of forms; the most frequent is the round, measuring 5 to 10 μ; many minute ones of the same kind are seen, 2 to 3 μ in diameter, often in clusters; budding forms are frequent and others making a figure of 8. Another frequent appearance is the rod-like one with rounded ends. Some forms are elongated and in phantastic shapes. These organisms stain with difficulty, a faint rim of blue being often all that can be seen with the modified Gram's stain. No internal structures have been made out, nor is any evidence of sporulation seen except in cultures.

In sections the organisms are found in small numbers in the types A and B, in the more superficial layers of epithelium between the cells. We have found no differential stain for them. With hæmatoxylin and eosin they stain to a light brown and often have a halo about them. They are most readily demonstrated (fig. 10) in unstained sections treated with potassium hydroxide and mounted in glycerin. The double contour is then fully brought out and this, with buds, makes identification certain. In type C they are found more deeply in the section, but always among the epithelial elements.

Scales from type A failed to yield a culture although when incubated for a week and examined they showed a great increase, with elongation and segmentation of the organisms which approached the cultural forms seen in fig. 12. Scales from type B were washed in water, soaked in absolute alcohol one hour, washed in salt solution and put on plates and slants of maltose and glucose agar. Many remained sterile, a few showed a subtilis-like organism; one on glucose agar, after four days' incubation, gave a filamentous growth in pure culture. This culture on being transplanted grew more readily on sugar media and potato, but showed only a slight filamentous growth on plain and glycerin agar either at room or body temperatures.

The organism grows on potato, at room temperature, in prominent, light brown folds (fig. 10). At body temperature the folds are black. Microscopically (fig. 11) the growth consists of short, blunt branching and segmented processes and in round forms, 20 to 30μ in diameter filled with a number of small, round spores.

The growth on glucose-agar is abundant, forming brown folds in the center and lighter filamentous processes at the edges. No aërial spore-bearing hyphæ are seen. Microscopically (fig. 13) the processes are longer, more slender and no sporulating forms are seen.

The development on maltose-agar is less marked and consists of a brown film on the surface and a white growth penetrating deeply into the medium (fig. 13).

In glucose-bouillon a floculent white ball is found at the bottom of the tube; the fluid above is clear. A slight liquefication occurs in gelatin. Milk is coagulated, but not acidified. No fermentation takes place in lactose, glucose and maltose tubes.

No marked difference in the growth appears at room and body temperatures, except in its color on potato which is noted above.

This organism when injected subcutaneously in guinea pigs, produces a small nodule which soon disappears; double contoured budding bodies are found in the substance of the nodule. On injection into the peritoneum similar nodules are found in the omentum which contain round forms and remains of the filamentous growth injected.

A growth was obtained from type C in the same way, although most of the tubes remained sterile. This growth shows a preponderance of yeast-like forms in the center of the culture with filaments at the edges; the center often retains Gram's stain, while the margin stains brown.

On agar a brownish-black, pasty growth with lighter colored filamentous borders appears along the track of the needle. Growth is not abundant (fig. 14).

Glucose-bouillon gives numerous filamentous islands of growth in the body of the tube with a brown film at the surface. Glucose, lactose and maltose are not fermented. There is no change with milk. Potato gives a pasty black growth with folds. Glucose and maltose show an abundant, brownish-black, pasty growth with lighter colored filamentous edges. Injections into the peritoneal cavity of guinea-pigs were negative.

V. OTHER FORMS OF BLASTOMYCOSIS.

This disease of the skin is especially interesting in view of the presence in these Islands of a blastomycotic disease of horses and of the finding of blastomycetes in ulcers, in sprue and allied diseases.

Strong, in 1904, identified as blastomycotic a disease of horses known as pseudo farcy or ulcerative lymphangitis. He obtained only a slight growth at that time. A similar disease has been known for some time in Italy, France, Algiers, Russia, and Japan. It was more prevalent in Manila in 1903 and 1904 than at present, but we have seen several good cases. Fig. 14 shows a horse which we observed at the ice plant through the courtesy of Veterinarian Bishop. Veterinarian McKinnen, quartermaster's department, kindly sent us some sterile pus from a native pony and this after a month on glucose-agar, gave a slight growth. On transplantation this grew more readily on the same medium, but slowly on maltose-agar and potato. Figure 15 shows the convoluted, brown growth on maltose-agar. At room temperature the slow, new growth at the edges is pure white. Microscopically (fig. 17) it shows branching, segmented hyphæ with rounded ends and a great many free, round forms. The organisms in the ulcerating lymph-glands are oval, and are more uniform in shape and size than those in the skin disease; the membrane is not as distinct. The cultural characters are also very different. However, in order to determine if possible the question of relationship, two horses were inoculated subcutaneously, one with scales of the second form of disease, and one with the culture obtained from the third form; no infection resulted.

We have seen no general infection with blastomycetes, but think it probable that such cases exist in the Islands. We have had a Scout sergeant under observation with a good history and who was otherwise healthy, who suffered from gradual loss of weight, with cough, spitting of blood and pain in the chest. No tubercle bacilli could be demonstrated by repeated examinations or by inoculation; no ova were present in the sputum. Blastomycetes, however, were found in large numbers. The patient recovered completely in two months on ascending doses of potassium iodide. We have seen several cases like this one, but have not been able to satisfy ourselves entirely that the blastomycetes were pathogenic or to obtain encouraging cultures. However, we believe that lung infection may occur and may explain many obscure cases.

Dantec has recently stated that sprue is a blastomycosis of the intestinal tract and we have found numerous blastomycetes in two cases of sprue seen since reading Dantec's article. In two cases of hill diarrhœa we have encountered large numbers of blastomycetes in the stools and using Dantec's technic have obtained the same culture from each case. The growth is white, powdery, with a pasty center consisting of yeast-like forms and filamentous borders. This subject will be reported upon at length later. The ulcerations as reported by Strong, Sakurane and Okugawa in which blastomycetes have been found were undoubtedly due to these organisms. Those described by Strong resemble more closely the organisms from the horse than those which we have described. No definite description of the organisms is given by Sakurane and Okugawa. The patient was a Japanese girl age 9 who had three ulcerating nodules on the face and nose and an enlarged submaxillary gland. Cultures from all the lesions were black, with gray filamentous edges and consisted mostly of yeast-like bodies which grew best on sugars.

VI. CONCLUSION.

In the Philippines a blastomycotic infection of the skin is one of the common dermatologic findings. It exists in at least three forms, two of which are milder than those seen in the United States. It is usually unrecognized; in the milder forms it is taken to be ring-worm or some form of dhobie itch; in severer types it is diagnosed as tuberculosis or syphilis. The milder types yield to local antiseptics, the more chronic and severe only to potassium iodide given internally. Further development of the subject will be necessary before these types, as well as those found in horses, in ulcers, in sprue and hill diarrhœa can be definitely classified.

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Strong, *This Journal* (1906), **1**, 91.
Shattuck, *This Journal, Sec. B.* (1907), **2**, 551.
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Dantec, *Bulletin de Société Pathologique* (1908), I, **6**, 342.

ILLUSTRATIONS.

PLATE I.

FIG. 1. Case I.
2. Lesions of four months' duration on nose and border of jaw.
3. Case V.
4. Case VI.

PLATE II.

FIGS. 5 and 6. Blastomycetes in scales, Case I, × 560.
FIG. 7. Section of skin, Case I, × 40.
8. Section of skin, Case V, × 50.

PLATE III.

FIG. 9. Section of skin, Case V, × 400.
10. Potato culture, Case IV; maltose-agar, growth from horse.
11. Growth on potato, × 350; Case IV.
12. Growth on maltose-agar, × 270; Case IV.

PLATE IV.

FIG. 13. Growth on maltose-agar Case IV.
14. Growth on agar; Case V.
15. Horse with ulcerative lymphangitis of neck.
16. Growth on glucose-agar, from horse; × 300.

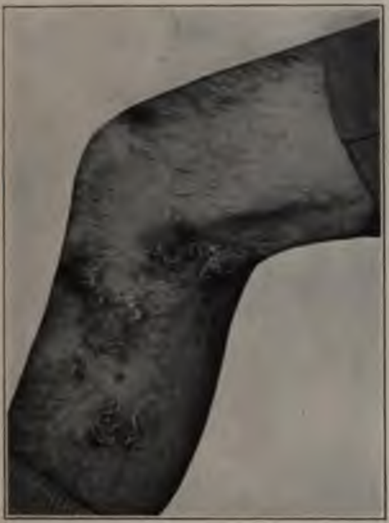


FIG. 1.

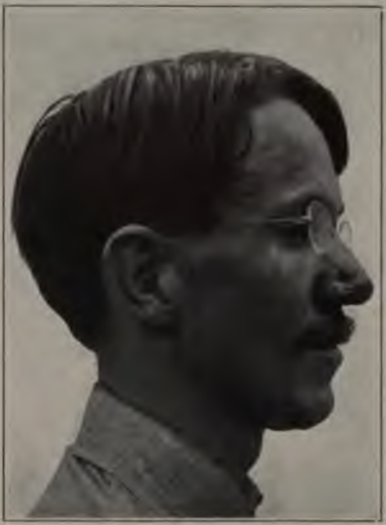


FIG. 2.

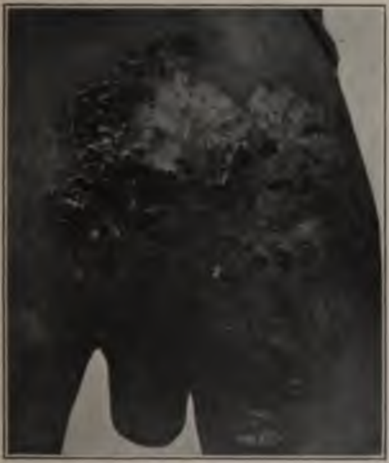


FIG. 3.

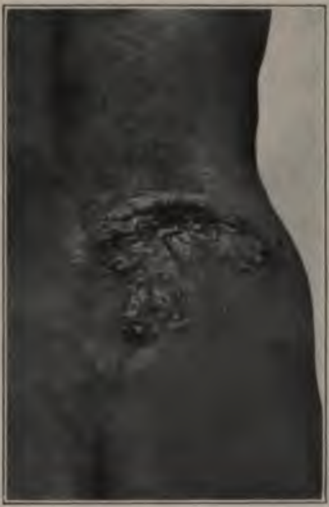


FIG. 4.

PLATE I.

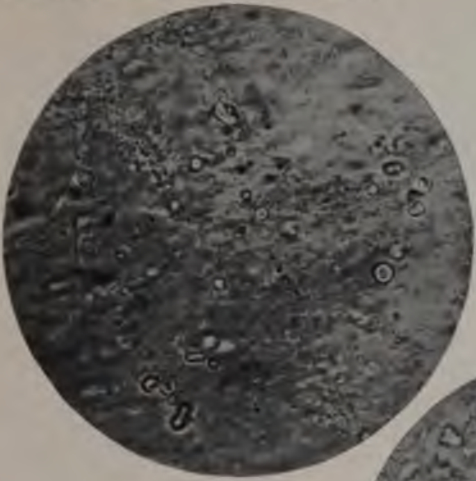


FIG. 5.

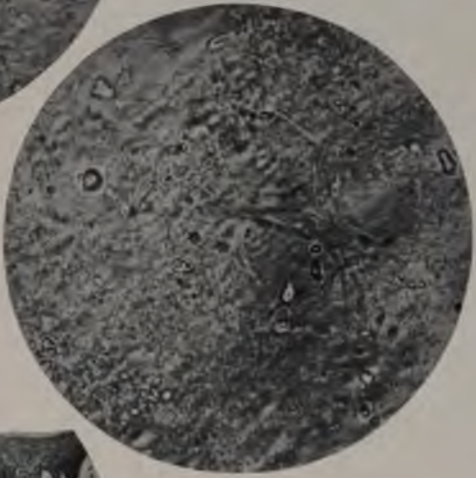


FIG. 6.

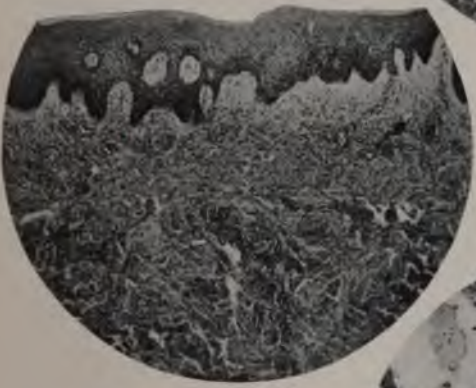


FIG. 7.

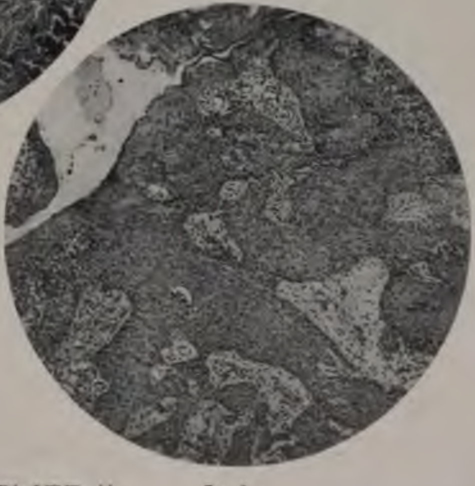


PLATE II. FIG. 8.

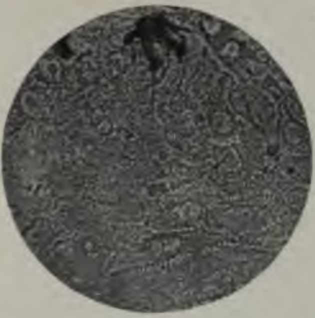


FIG. 9.

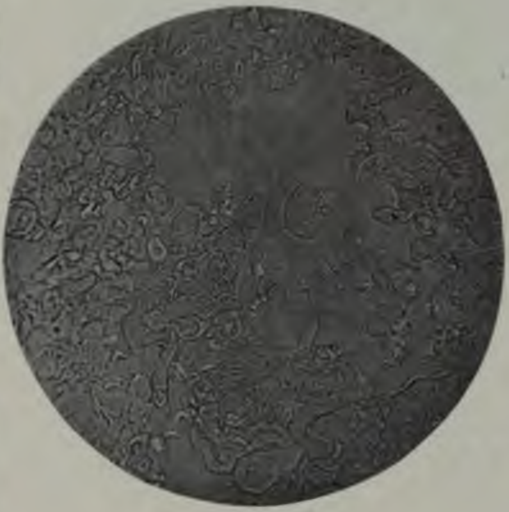


FIG. 11.

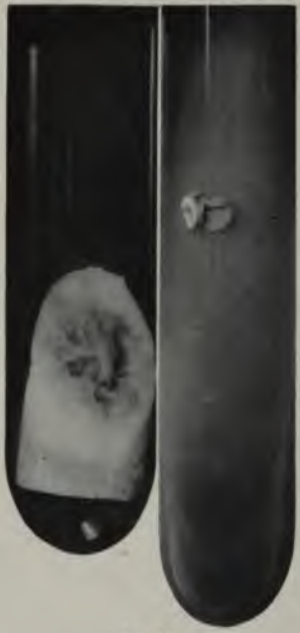


FIG. 10.

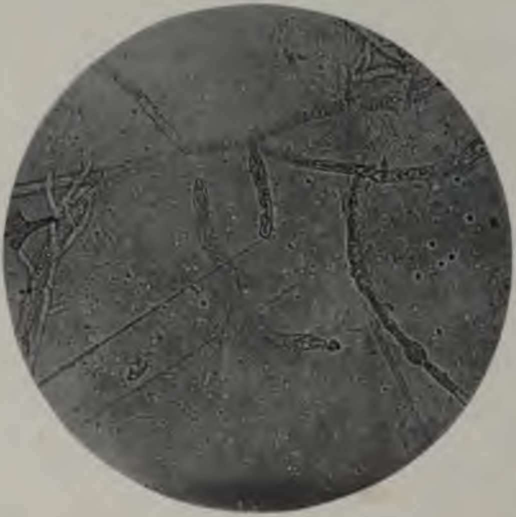


FIG. 12.

PLATE III.

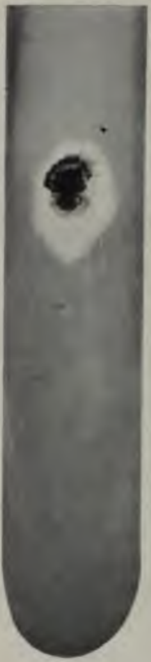


FIG. 13.

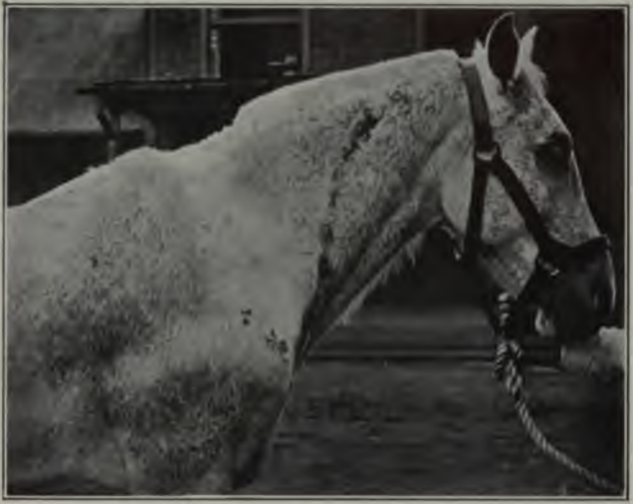


FIG. 15.

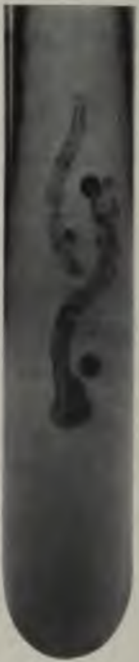


FIG. 14.

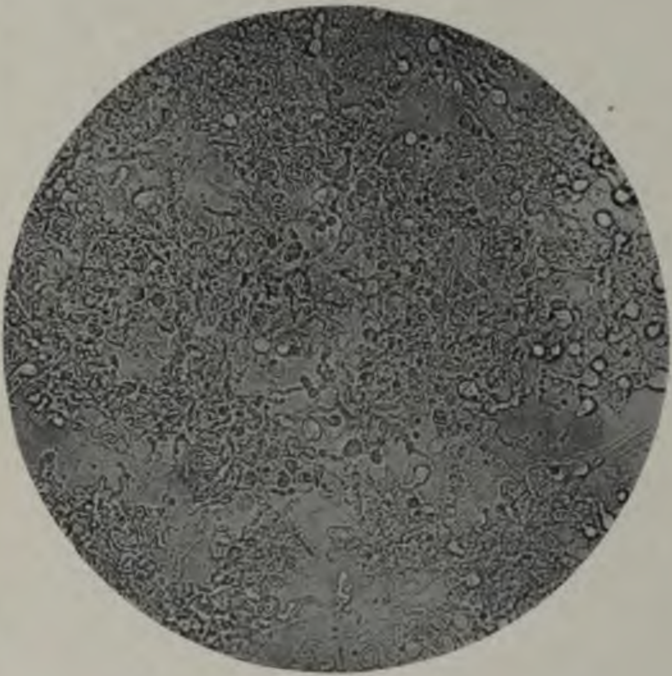


FIG. 16.

PLATE IV.

A REDUCTION IN THE COST OF ANTICATTLE-PLAGUE SERUM.

By E. H. Ruediger.

(From the Serum Section, Biological Laboratory, Bureau of Science, Manila, P. I.)

The cost of virulent material used in the preparation of serum against cattle plague is a question of great importance and one which has attracted my attention during the past few years. Numerous attempts to cultivate the specific organism of this disease have been futile, and it has been found necessary to adhere to the old method of bleeding to death bullocks suffering from cattle plague and to inject their blood, commonly known as virulent blood or V. B., into the animals to be immunized for serum purpose.

The average cost per bullock used for virulent blood is 50 pesos, Philippine currency (25 dollars, United States currency), and each bullock yields about five liters of blood, the carcass being waste; therefore, each liter of virulent blood costs 10 pesos.

In the course of the experiments carried on with filtrates of cattle plague material, I was deeply impressed (on repeating the experiments of Nicolle and Adil-Bey) by the high virulence of the artificial peritoneal fluid. The virulence of the peritoneal fluid seemed to be greater than that of the blood.

Having thoroughly convinced myself that the artificial peritoneal fluid is highly virulent, I requested Doctor Shealy of the Bureau of Agriculture, Manila, P. I., to inject 5 liters of a 0.5 per cent solution of potassium citrate into the peritoneal cavity of the sick bullocks, to bleed them to death an hour later, and to collect the peritoneal fluid and use it in immunizing serum animals.

Two series of animals, X and Y, were immunized for serum. The bullocks in series X received subcutaneous injections of artificial peritoneal fluid and the bullocks in series Y received subcutaneous injections of virulent blood. After having been well immunized the bullocks were bled for serum. The serum derived from the bullocks in series X was designated as serum X and that derived from the bullocks in series Y was designated as serum Y.

Ten bullocks, nonimmune to cattle plague, were now divided into two series, X and Y, with five bullocks in each series. The potency of serum X was determined on the bullocks in series X, and the potency of serum Y on the bullocks in series Y as follows:

SERIES X.

Five bullocks, numbered 78, 79, 80, 81 and 82, received 0.5 cubic centimeter of virulent blood injected under the skin and varying quantities of serum X.

Bullock No. 78, used as control, received no serum and died of cattle plague on the tenth day after inoculation. (Chart No. 78.)

Bullock No. 79 received 15 cubic centimeters of serum X. It went through an attack of cattle plague of moderate severity and recovered. (Chart No. 79.)

Bullock No. 80 was given a subcutaneous injection of 30 cubic centimeters of serum X. On the fifth day after inoculation reaction manifested itself by a rise of temperature. On the eleventh day the temperature dropped to normal and the animal made an uneventful recovery. (Chart No. 80.)

Forty-five cubic centimeters of serum X was injected into bullock No. 81. Five days later the temperature rose to 40°.5 C., but soon dropped to normal and the animal recovered without having shown any clinical signs of cattle plague. (Chart No. 81.)

Bullock No. 82, having received a subcutaneous injection of 60 cubic centimeters of serum X, showed a more marked reaction than did bullock No. 81 with the smaller dose of serum. Clinically he had loss of appetite for a few days. Diarrhœa never set in and recovery was rapid. (Chart No. 82.)

SERIES Y.

Bullocks numbered 83, 84, 85, 86 and 97, were each inoculated with 0.5 cubic centimeter of virulent blood and received varying quantities of serum Y.

Control bullock No. 83, which did not receive any serum died on the eighth day after inoculation. (Chart No. 83.)

Bullock No. 84, having received 15 cubic centimeters of serum Y, developed typical cattle plague and died on the tenth day after inoculation. (Chart No. 84.)

Thirty cubic centimeters of serum Y were injected under the skin of bullock No. 85; this animal died of cattle plague on the fourteenth day after inoculation. (Chart No. 85.)

Bullock No. 86 received an injection of 45 cubic centimeters of serum Y. After passing through a reaction of moderate severity, this animal made an uneventful recovery. (Chart No. 86.)

Bullock No. 87, having received 60 cubic centimeters of serum Y, had rather a severe reaction. Diarrhœa set in on the eleventh day after inoculation and continued throughout the twelfth day. On the twelfth day the temperature dropped to normal and remained normal; the diarrhœa suddenly subsided and rapid recovery followed. (Chart No. 87.)

CONCLUSIONS.

1. On comparing the results obtained with serum X with those obtained with serum Y, it was found that serum X had by far the higher potency.

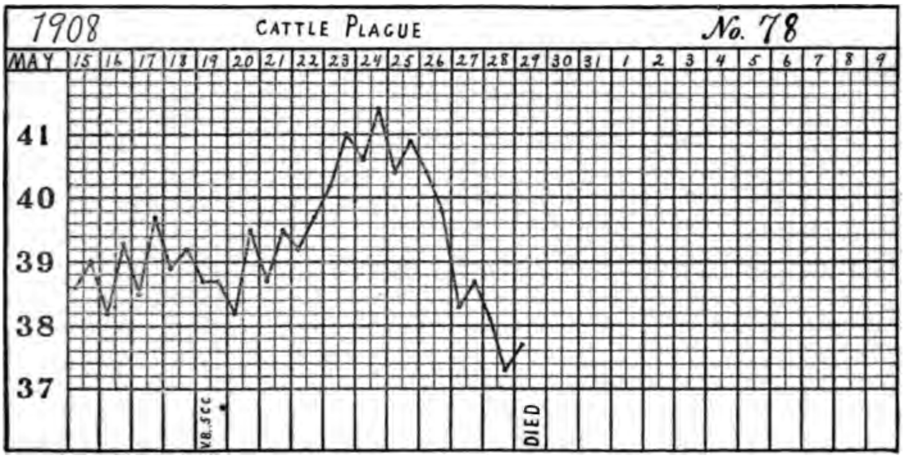
2. The quantity of virulent material used for inoculating serum

animals can readily be doubled by injecting one-half of one per cent solution of potassium citrate into the peritoneal cavity of the virulent blood animal and collecting this artificial peritoneal fluid after the animal has been bled to death.

3. The bullocks here used for virulent blood weigh between 200 and 250 kilos, each costs 50 pesos and yields about 5 liters of blood, each liter of blood costing 10 pesos. Since using the artificial peritoneal fluid, we obtain 5 liters of blood and 5 liters of peritoneal fluid, in all 10 liters from each bullock, at a cost of 5 pesos per liter.

ILLUSTRATIONS.

Chart Nos. 78 to 87.


1908
CATTLE PLAGUE
No. 78
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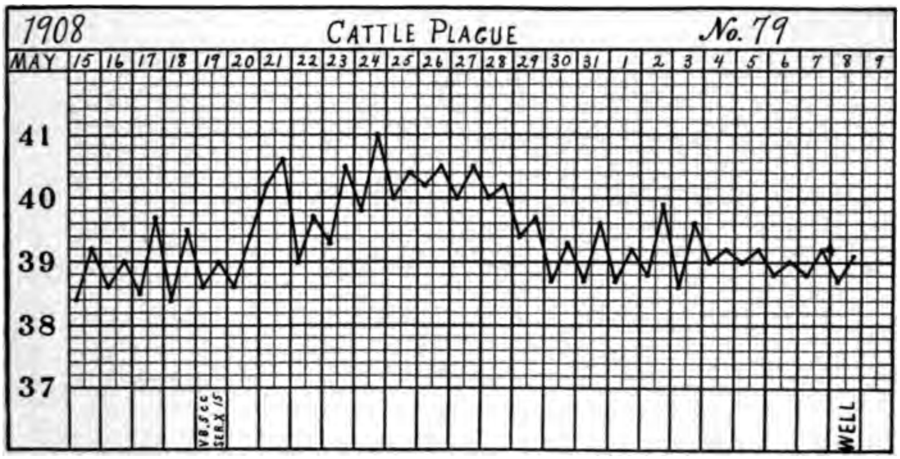
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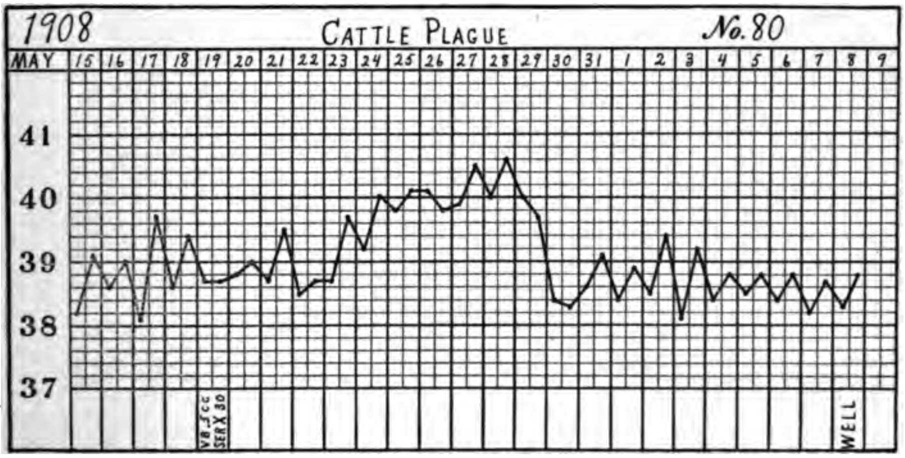
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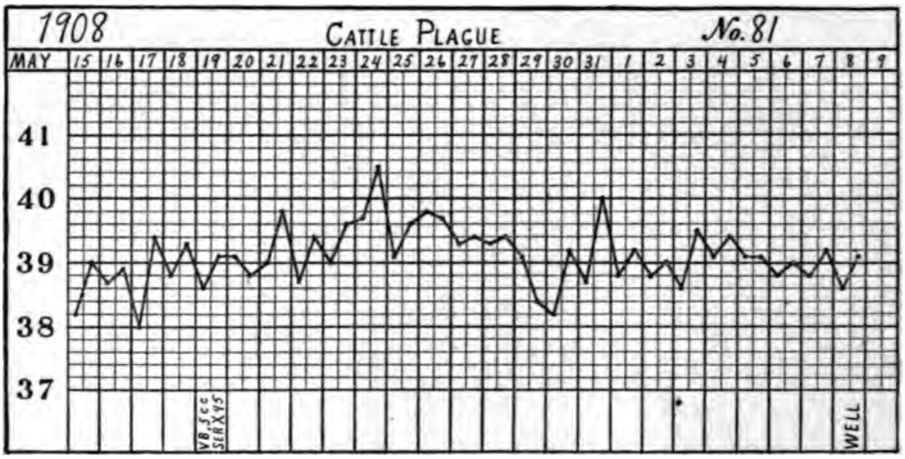
WELL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CATTLE PLAGUE
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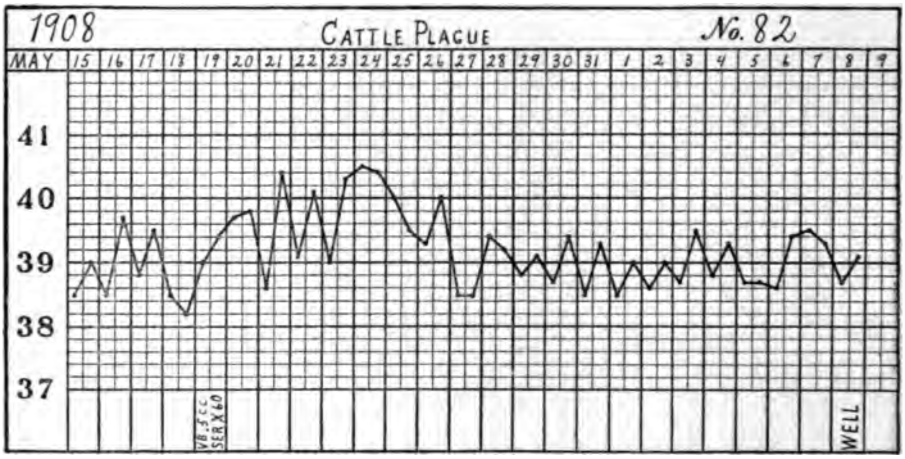
WELL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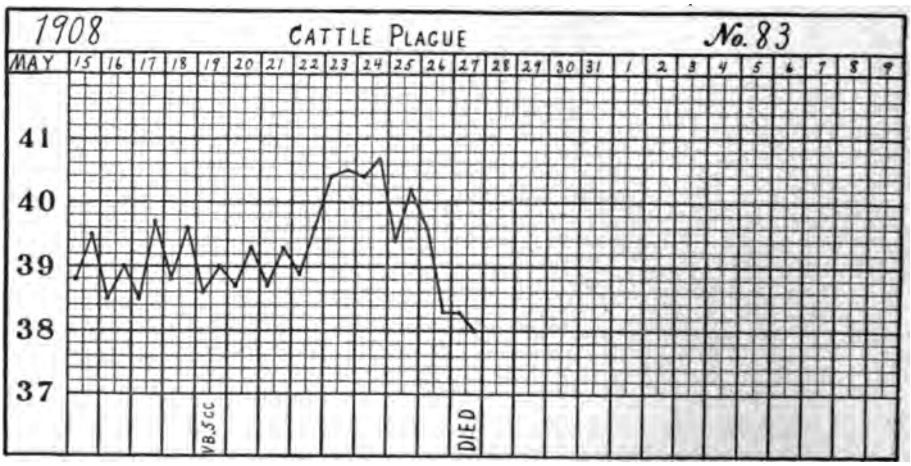
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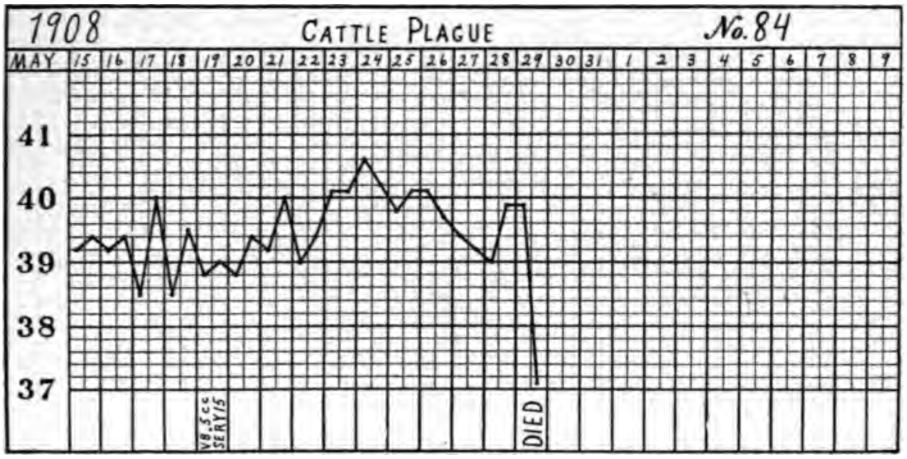
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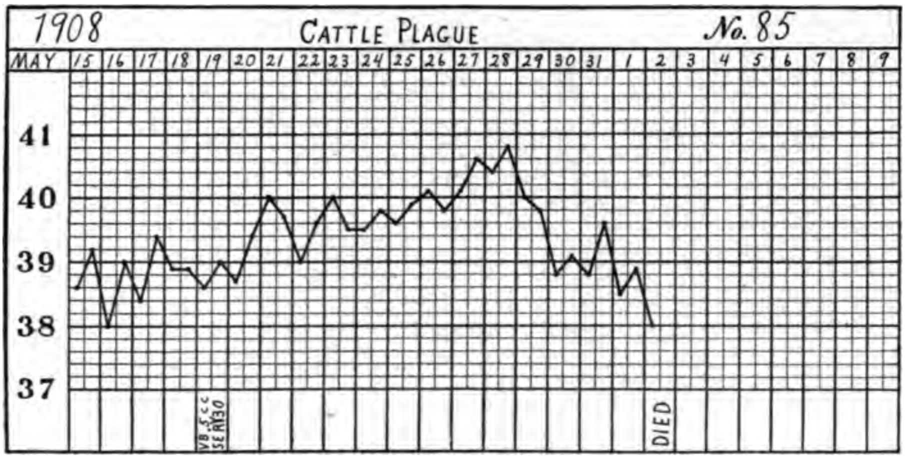
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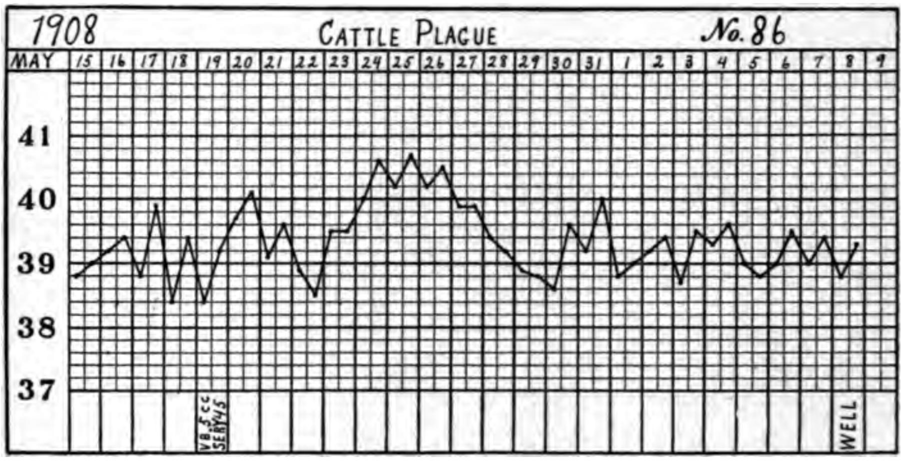
DIED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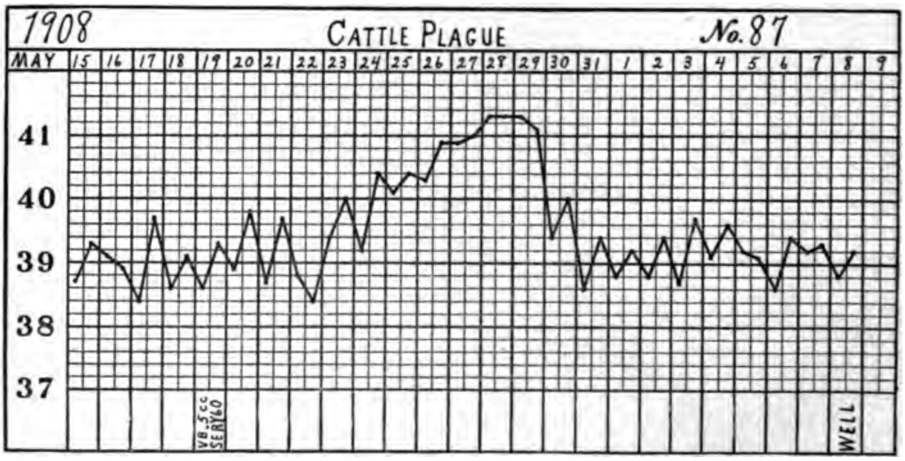
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VB. 5cc SERY60
WELL

RESULTS OF THREE HUNDRED EXAMINATIONS OF FÆCES WITH REFERENCE TO THE PRESENCE OF AMŒBÆ.[1]

By R. E. Hoyt.[2]

Microscopic examination of fæces was made a part of the regular laboratory routine at the Cañacao Naval Hospital in October, 1907, for the purpose of obtaining statistics as to the frequency of amœbæ and other intestinal parasites in the stools of officers and enlisted men of the Navy. Three hundred of these examinations were recorded in the latter part of November and the percentages given below are based on the findings in these cases. Records were also kept of blood examinations made from the first 200 patients whose fæces were examined, for the purpose of detecting or confirming any relation between blood findings and intestinal parasites. An occult blood test was made from the last three hundred cases with a portion of the fæces.

In order to make these stool examinations as nearly under the same conditions as possible, the following routine was carried out:

> On the morning after admission a saline cathartic was given to those patients whose condition did not contraindicate its use. The first liquid stool was then sent to the laboratory for examination. Blood films from the patients whose fæces had been examined were then prepared, a differential white count made, the presence of parasites recorded, and in cases which indicated other blood disturbances, further tests were made, such as estimation of hæmoglobin, counts of red cells, etc. The chloroform, tincture of guaiac and turpentine test for occult blood was made in the last hundred cases examined.

It has been the opinion at this hospital that a distinction between the so-called *Entameba hystolotica* and *Amœba coli*, based on the points of difference first enumerated by Schaudinn, is practically impossible where specimens of crude fæces only are examined. While organisms showing these distinguishing characteristics may perhaps be recognized where cultures are used and a comparative study made of them, the fact remains that it is extremely difficult to pick out these supposed points of difference with any degree of accuracy on film preparations of fæcal matter. Therefore, no attempt at differentiation has been made. Furthermore, as the fæcal mass often contains cells which, under the microscope, rather closely resemble non-motile amœbæ, specimens having positive amœboid movement at the time of examination have been recorded separately from those showing non-motile or encysted forms only.

---

[1] Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, Manila, P. I., February 27, 1908.

[2] Passed assistant surgeon, United States Navy.

Only 20 of the 300 patients whose stools were examined were admitted with the diagnosis of dysentery. Ten of these cases were either hospital corps men or medical officers stationed at the hospital, and in these cases the diagnosis was based more on the discovery of motile amœbæ in the stools than on any typical symptoms of dysentery.

About 45 per cent of the remaining cases might be classed as "medical," and these included fevers, chiefly malarial, dengue, and typhoid; mental and nervous diseases, diseases of the blood, intoxications and medical affections of the chest and abdomen. Diseases of the eye, ear, nose and throat were also placed in this group. Twenty-five per cent of the cases were "surgical" and included wounds, contusions, fractures, abscesses, tumors and the various surgical affections of chest and abdomen. Twenty-five per cent of the patients were afflicted with venereal diseases. Among all specimens of fæces examined, 104, or 34.6 per cent, contained motile amœbæ. Fourteen, or 70 per cent, of the specimens from the 20 patients admitted with dysentery were positive for amœbæ. Eliminating these 20 cases there remained 84, or 30 per cent, which gave positive evidence of motile amœbæ in the fæces, without showing at the time of examination any symptoms which could positively be attributed to their presence in the intestinal canal.

The following percentages were obtained as the result of these 300 examinations:

Motile amœbæ	34.6
Motile flagellates	15.3
Ova of *Ascaris lumbricoides*	10.0
Ova of *Trichocephalus dispar*	6.6
Ova of *Agchylostoma duodenalis*	3.3

Included in these 300 examinations were seventeen specimens from native Filipinos who were admitted to the hospital for various ailments, but only two were admitted for dysentery. The percentages of these cases are as follows:

Motile amœbæ	76.0
Ova of *Ascaris lumbricoides*	53.0
Ova of *Trichocephalus dispar*	76.3
Ova of *Agchylostoma duodenalis*	29.4

Subtracting these 17 cases from 300 and arranging the percentage for white enlisted men and officers of the Navy, the result is as follows:

Motile amœbæ	32.15
Ova of *Ascaris lumbricoides*	7.4
Ova of *Trichocephalus dispar*	2.5
Ova of *Agchylostoma duodenalis*	1.5

Sixty-six and two-thirds per cent of the dysenteric cases among white men showed positive evidence of motile amœbæ.

In addition to the records of motile amœbæ, an account was also kept of the presence of encysted and non-motile amœbæ, and in many cases where there was doubt of the identity of the organism the point was settled by examination with cultures. In 21 per cent of all cases examined either non-motile or encysted or both forms of the orgonism were found in preparations in which before no motile amœbæ could be detected. Allowing 5 per cent for possible error, there remains about 50 per cent of all cases examined showing evidence of amœbic infection.

An effort was made to discover from the first 100 cases some relation between length of service on the station and the presence of amœbæ in the intestinal canal, also any relation between sea and shore duty and infection.

From a total of 56 patients admitted from shore stations, station ships, torpedo boats and the smaller cruising vessels of the Philippine Squadron, from which the crew receive abundant liberty and were therefore often exposed to infection, 36 cases or 64 per cent showed positive evidence of amœbæ. Of 16 cases admitted from the larger cruising ships on which the men had spent one year on this or the China Station, 5 or 31 per cent were infected; of 21 patients admitted from the Armored Cruiser Squadron, which had been but four months on the station, 7 or 33 per cent showed amœbæ on examination. Sixty-five per cent of the patients admitted from strictly shore stations and 43 per cent of those admitted from strictly cruising ships gave positive tests for the organisms. Prolonged service on the station and continued residence on shore, therefore, as would naturally be expected, favors the chances of infection.

The examination of blood films, beyond showing a slight increase of eosinophiles in about 40 per cent of the cases containing amœbæ (over 5 per cent in 41 per cent of these cases) showed nothing remarkable. In nineteen preparations, malarial parasites were discovered, 13 from the blood of patients admitted with malaria and 6 from patients admitted with some other diagnosis.

The results of the tests for occult blood in the last 100 cases, while not conclusive in any way, are nevertheless interesting. Of the total of 35 cases found positive for motile amœbæ, 71.4 per cent gave a positive occult blood test. Seven of these cases were admitted with the diagnosis of dysentery; the others with diseases in which blood in the fæces would not be expected. In only 6 per cent of the remaining 65 cases was the test positive, the reaction being obtained in two *Agchylostoma* and one flagellate infection, and in one case of gall stones with cholocystitis.

During the eight months these examinations have been conducted, seven hospital corps men stationed at the hospital and three medical officers have been infected with amœbæ, although rigid precautions against such an accident were taken. In spite of the use of distilled water, cooked vegetables and carefully disinfected fruits, infection has occurred, and it can therefore easily be understood how simple a matter it is for men who are stationed on shore in this vicinity and who take absolutely no precaution against the disease, to become infected in a comparative short time.

As before mentioned, while these officers and hospital corps patients were admitted to the sick list with the diagnosis of dysentery, the typical signs and symptoms of dysentery in nearly all cases were absent and the diagnosis was based chiefly on the results of stool examinations and lack of other evident cause for the symptoms present. As a rule, these symptoms began with gradually increasing debility, loss in weight and strength, anæmia, and in some cases digestive disturbances of various sorts; indigestion, slight diarrhœa or constipation and uneasy feelings over the region of the colon. In a few cases a mild neurasthenic state developed. Blood and mucus were not present in the stools and complaints of tenesmus were not made in these cases. Antidysenteric treatment (chiefly high irrigations of the colon), while causing an apparent relief of symptoms in some cases for a short time, resulted in no permanent good and eventually the patients whose terms of duty did not expire within the eight months, were surveyed and sent to the United States.

Some few of the other patients admitted to the hospital with diagnosis other than dysentery gave histories somewhat similar to those described above, and such symptoms as debility, anæmia, loss in weight and strength and digestive disturbances could not be accounted for by the diagnosis on admission. In these cases the physical and laboratory examinations would fail to give any more positive results than the presence of motile amœbæ or flagellates in the stools. Many of these cases also seemed to be temporarily benefited by high irrigations of the colon.

It is uncertain as to whether the presence of amœbæ plays any part in the causation of these symptoms or whether they are unfavorably influenced by a tropical climate, as is commonly believed; but reasoning from a knowledge of the power of other forms of intestinal parasites to produce symptoms of a general nature, such as those already mentioned, and taking into consideration the reported findings at autopsy in many cases of amœbic infection without apparent symptoms of dysentery, it would be very unwise to ignore this organism as an etiologic factor in affections other than typical dysentery.

THE INOCULATION OF BACTERIAL VACCINES AS A PRACTICAL METHOD FOR THE TREATMENT OF BACTERIAL DISEASES, WITH SPECIAL REFERENCE TO THE TREATMENT OF INFECTIONS DUE TO THE GONOCOCCUS.[1]

By EUGENE R. WHITMORE.[2]

None of us would think of treating a case of diphtheria without antitoxin, any more than we would think of opening an abdomen without taking precautions as to asepsis. It will undoubtedly be a surprise to many when I say that we are all neglecting every day a well founded method of treating a much larger class of bacterial diseases than the one that yields to antitoxins; and all earnest workers who are using this method, opsonotherapy, are obtaining as surprisingly good results as we get from antitoxin in diphtheria.

The great amount of literature that has been produced on Ehrlich's theory, the voluminous discussions on aggressins, agglutinins, precipitins, etc., the great amount of theoretical work on serum therapy, and the publication in the United States of a number of technical and abstruse papers on opsonotherapy, have made the every day physician lose all interest in discussions on biologic medicine. It is quite probable that too much stress has been placed on the taking of the opsonic index and it is possible that the theory may have to be modified, but the method of treatment based on this theory is giving results that are little short of wonderful.

Denys observed, in 1895, that in rabbits immunized against a virulent streptococcus, the leucocytes possessed markedly increased phagocytic power toward those cocci, as compared with the leucocytes of a normal rabbit. Several investigators confirmed this finding and Mennes showed that the same thing is true for the pneumococcus. Since that time considerable work has been done along this line, and several methods of bacteriologic diagnosis, notably the Widal reaction, have been developed on the basis of the detection of the products of immunity developed in the blood as the result of auto-inoculation.

Many investigators, notably Metchnikoff, claimed that the increased phagocytic power of the leucocytes when mixed with the immune sera was due to a direct stimulation of the leucocytes. Wright and his assistants showed that the same phenomenon was not a result of the stimulation of the leucocytes, but is caused by an increase of some element in the blood which acts directly on the bacteria and so alters them that the leucocytes are able to ingest them. To these substances (for he showed that they were multiple) he gave the name of "opsonins." Thus, as Ohlmacher puts it, "it remained for Wright so to modify the vaccine of Pasteur as to arouse in the serum of Buchner a substance which prepared the disease producing microbe for ingestion by the phagocyte of Metchnikoff; thus bringing to practical humanitarian usefulness the laboriously studied theories of these pioneers in biologic therapy."

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[1] Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, Manila, P. I., February 27, 1908.

[2] Captain and assistant surgeon, United States Army; pathologist, Division Hospital, Manila.

While Wright's work and his results have been well known for about four years, his method of treatment has been considered too technical for the average worker, and on this account it has not received the general consideration that it merits. It is not my intention to enter into a discussion of the principles of opsonotherapy, but I desire to urge that it is a practical method for the treatment of certain bacterial diseases, and the practice is the truly valuable condition we have in opsonotherapy.

Wright enumerates "the methods, other than vaccine therapy, which we have today for the treatment of bacterial diseases, as: (1) chemical antiseptics; (2) extirpation of the focus of infection; (3) the determination of lymph to the focus of infection; (4) sero-therapy; and (5) expectant treatment."

The mere enumeration of these methods calls to the mind of every one of us numerous failures, and how in any case these methods leave the issue more or less to chance.

Before proceeding to a discussion of the practical application of vaccine therapy it will be well for us to review the methods used by the body in the prevention and cure of bacterial disease.

(*a*) Mechanical covering. This is of comparatively slight importance.

(*b*) The main constituents are the antibacterial elements in the blood. These are (1) bacterial substances, which kill bacteria; (2) bacteriolytic substances, which kill and dissolve bacteria; (3) agglutinins, which agglutinate bacteria; and (4) opsonins, which alter the bacteria so that they are readily ingested and digested by leucocytes. In this connection the leucocytes must be considered as of great importance.

(*c*) The body is able to manufacture antitoxins which do not necessarily affect the invading bacteria, but neutralize the toxins produced by these bacteria.

The body combats bacterial invasion in two ways: The first and most important, by attacking the bacteria themselves and the second by neutralizing the toxin produced by the bacteria. The diphtheria bacillus is the shining light among the organisms which stake their existence against an antitoxic combat; while the tubercle bacillus, the pyogenic cocci, including the gonococcus, the pneumococcus, the typhoid bacillus and a number of others stake their existence against an opsonic combat.

Failure to recognize these different methods by which the body combats bacterial invasion has been the cause of many bitter disappointments in the field of serum therapy.

So far it has been impossible to demonstrate any increase of opsonin for the diphtheria bacillus by inoculation with the dead bacteria. Practically, however, it would seem that some antibacterial element must be developed, or increased, for it is hard to understand why the local condition ceases so promptly and why the diphtheria bacillus regularly, though slowly, disappears from the throat if the reaction is purely antitoxic. On the other hand, it seems probable that some antitoxin is produced against the bacteria that are mainly attacked by opsonins. This would account for some of the partial successes achieved in the antitoxic treatment of bacterial diseases that are now known to belong in the opsonic army.

Again to quote Wright's words, "it is only when bacteria or their products enter the blood and endanger life that nature addresses herself seriously to the task of immunization. As long as a bacterial invasion is purely local, nature opposes to it no more than a passive resistance." This is an important generalization and we at once see that it is the key to the situation in lupus, acne, furunculosis, gonorrhœal arthritis, epididymitis, urethritis, conjunctivitis, and a number of other infections. Further, the production of antibacterial and antitoxic substances following inoculation is a local process at the site of the inoculation.

With these few remarks on the physiology of immunization, we can proceed to a discussion of the specific application of vaccines in the treatment of bacterial diseases. In order that we may successfully combat bacterial invasion by use of its opsonins which are normally present in the blood, two things are necessary: (1) the opsonins must attack the bacteria and so alter them that they can be ingested by the leucocytes; (2) the leucocytes must ingest and disintegrate the bacteria. This at once gives us the key to the opsonic index which, in the case of bacterial disease, is an index to what nature is doing toward immunization against the specific bacterium. "Taking the opsonic index" is a fairly technical procedure and has been the main stumbling block in the practical use of opsonotherapy. It was not my intention to describe the means of taking the opsonic index, but there seems to be so much misunderstanding about it that I will give the method used in practical work.

Ordinarily the bacteria are grown on agar. The gonococcus does not grow on this medium, so I have cultivated it by taking a drop of blood from a man's ear in the usual way, smearing the blood over the surface of a plain agar or a glycerine-agar tube and making my culture on it. I have made hundreds of cultures in this way during the past twenty months and have very rarely had a contamination. It is also very easy to obtain a pure culture of the gonococcus in this way from an early case of urethritis. I have been able to induce some strains of the gonococcus to grow on glycerine-agar after a long time.

Equal volumes of the patient's blood (from say a case of gonorrhœal arthritis),

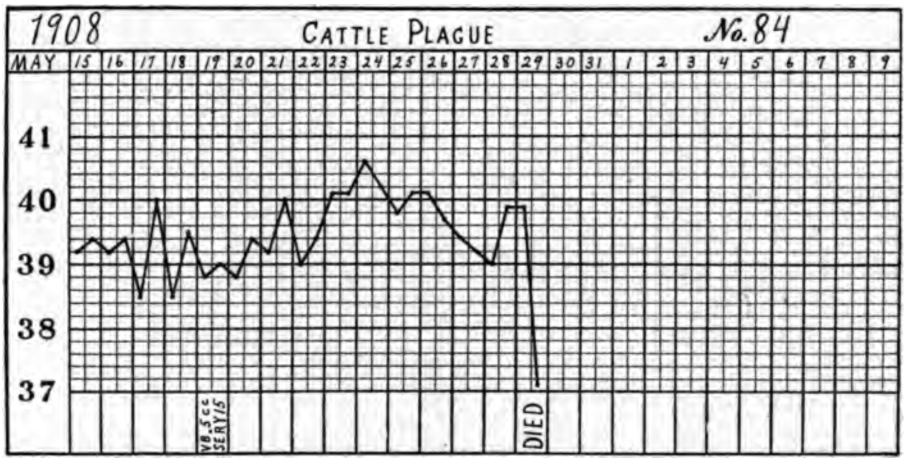
drawn directly from the ear; a 1 per cent sodium citrate solution in normal salt; and a normal salt emulsion of a young culture of gonococcus, are mixed in a pipette and put in the incubator at 38° for twenty minutes. At the end of this time the mixture is blown out on slides, stained, and the number of cocci ingested by, say, 100 leucocytes are counted and averaged. Suppose the average is two. Exactly the same procedure is gone through using a normal man's blood instead of the patient's. Perhaps here the average is four. This normal man's opsonic index is taken as 1. So, since the average number of cocci taken up by the patient's leucocytes is one-half the average number taken up by the normal man's blood, it follows that the patient's opsonic index is 0.5.

We see that the opsonic index is purely a matter of relative amounts of opsonins in two samples of blood, one of which is normal. The temperature at which the reaction is carried on may vary from 37° to 39° and the time from fifteen to thirty minutes, but both bloods must be treated exactly alike as to temperature and time.

I will not enter into a discussion of Simon's method of determining the percentage of phagocytic leucocytes, or the relative merits of the two methods. One of my main objects, as I said above, is to impress the fact that the taking of the opsonic index has nothing to do with the actual treatment of the case; that in certain bacterial diseases, enough has been done to place opsonotherapy beyond the experimental stage; and that the dosage has been determined accurately enough so that the vaccine can be inoculated and the results of treatment determined by the progress of the case. Thus, while the determination of the opsonic index is the only scientifically accurate method of following the effect of the inoculation, practically, in some diseases the progress of the case is a sufficient guide as to the effects of the treatment. Again, since it has been shown that killed cultures of bacteria retain their opsonin producing properties for weeks, the actual manufacture of the vaccine is not a necessary part of the treatment of a particular case.

Wright used Koch's new tuberculin in the treatment of local tuberculosis. Burroughs, Wellcome and Company have placed on the market vaccines for use against typhoid and staphylococcus infections. Suppose we have a case of furunculosis to treat. Enough work has been done already on furunculosis so that we can be sure of obtaining a pure culture of *Staphylococcus aureus* from the furuncles in our case and of finding our patient's opsonic index low for that particular coccus; we can also be certain that the inoculation of half a billion to one billion dead staphylococci of this strain would cause a rise in our patient's opsonic index and at the same time the furunculosis would clear up. This being the case, it is necessary to obtain a tube of *Staphylococcus aureus* vaccine, inject the proper dose, as given on the tube, and determine the result by the progress of the case.

Thus we see that the taking of the opsonic index is one separate manipulation and the preparation of the vaccine is another, and the only absolutely essential step in the treatment of any case of certain of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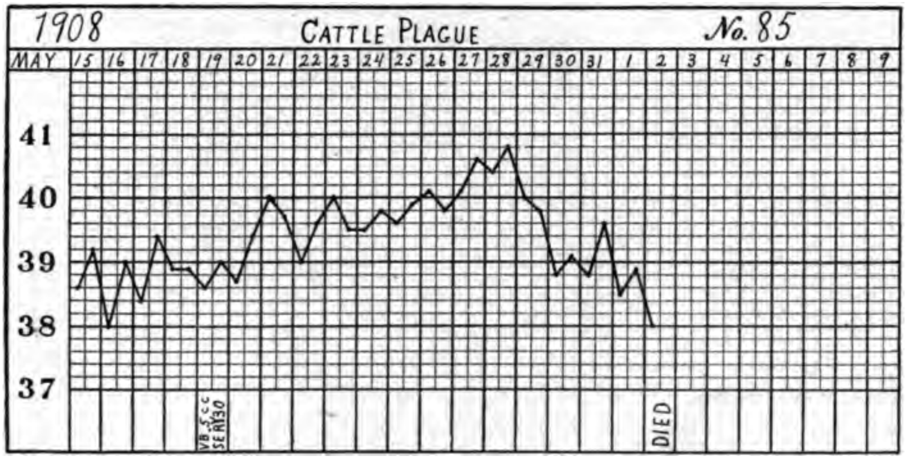
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Other cases of gonorrhœal arthritis, furunculosis, acne, empyema and lupus have given excellent results. I have just injected a refractory case of *Pemphigus contagiosa* with vaccine from the pustules of the patient and the outcome, apparently, will be satisfactory.

The result in gonorrhœal ophthalmia should be good, and the ability to keep vaccine on hand would make it possible to start opsonic treatment at once without in any way interfering with the other treatment of the case. Ohlmacher reports good results in three cases.

SUMMARY.

(1) The opsonins are the most important of the antibacterial elements in the blood and opsonotherapy is one of our best methods for the treatment of an ever increasing number of bacterial diseases.

(2) Opsonotherapy has passed the experimental stage and since it has been shown that certain vaccines retain their potency for weeks, it is practicable to treat certain bacterial diseases by the injection of the corresponding vaccine, just as we treat diphtheria by the injection of the corresponding antitoxin.

(3) Gonorrhœal arthritis responds readily to inoculation with vaccine, and this condition is to be placed in the list of diseases which can be treated by a vaccine prepared commercially.

(4) Gonorrhœal epididymitis seems to respond readily to inoculation with vaccine, while, so far, no statement can be made regarding urethritis.

(5) The opsonic index, while it is the only scientifically accurate method of estimating the immunization response to bacterial inoculation, is not necessary in the treatment of certain bacterial diseases; the progress of the case being sufficient index for practical purposes in such diseases.

(6) Bacterial inoculation does not interfere in any way with any other treatment that it is desired to carry out in a particular case of any disease.

RESULTS OF THREE HUNDRED EXAMINATIONS OF FÆCES WITH REFERENCE TO THE PRESENCE OF AMŒBÆ.[1]

By R. E. Hoyt.[2]

Microscopic examination of fæces was made a part of the regular laboratory routine at the Cañacao Naval Hospital in October, 1907, for the purpose of obtaining statistics as to the frequency of amœbæ and other intestinal parasites in the stools of officers and enlisted men of the Navy. Three hundred of these examinations were recorded in the latter part of November and the percentages given below are based on the findings in these cases. Records were also kept of blood examinations made from the first 200 patients whose fæces were examined, for the purpose of detecting or confirming any relation between blood findings and intestinal parasites. An occult blood test was made from the last three hundred cases with a portion of the fæces.

In order to make these stool examinations as nearly under the same conditions as possible, the following routine was carried out:

On the morning after admission a saline cathartic was given to those patients whose condition did not contraindicate its use. The first liquid stool was then sent to the laboratory for examination. Blood films from the patients whose fæces had been examined were then prepared, a differential white count made, the presence of parasites recorded, and in cases which indicated other blood disturbances, further tests were made, such as estimation of hæmoglobin, counts of red cells, etc. The chloroform, tincture of guaiac and turpentine test for occult blood was made in the last hundred cases examined.

It has been the opinion at this hospital that a distinction between the so-called *Entameba hystolotica* and *Amœba coli*, based on the points of difference first enumerated by Schaudinn, is practically impossible where specimens of crude fæces only are examined. While organisms showing these distinguishing characteristics may perhaps be recognized where cultures are used and a comparative study made of them, the fact remains that it is extremely difficult to pick out these supposed points of difference with any degree of accuracy on film preparations of fæcal matter. Therefore, no attempt at differentiation has been made. Furthermore, as the fæcal mass often contains cells which, under the microscope,

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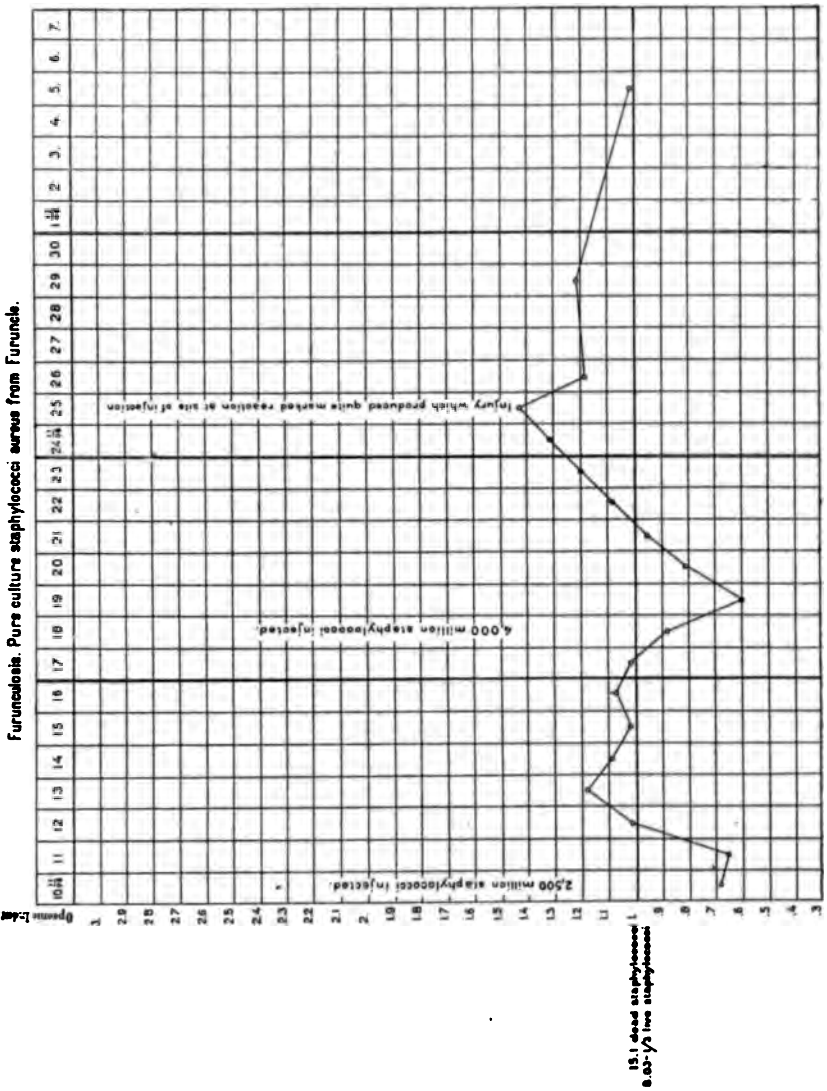
[1] Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, Manila, P. I., February 27, 1908.

[2] Passed assistant surgeon, United States Navy.


Furunculosis. Pure culture staphylococci aureus from Furuncle.
2,500 million staphylococci injected.
4,000 million staphylococci injected.
Injury which produced quite marked reaction at site of injection
Opsonic Index
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15.1 dead staphylococci
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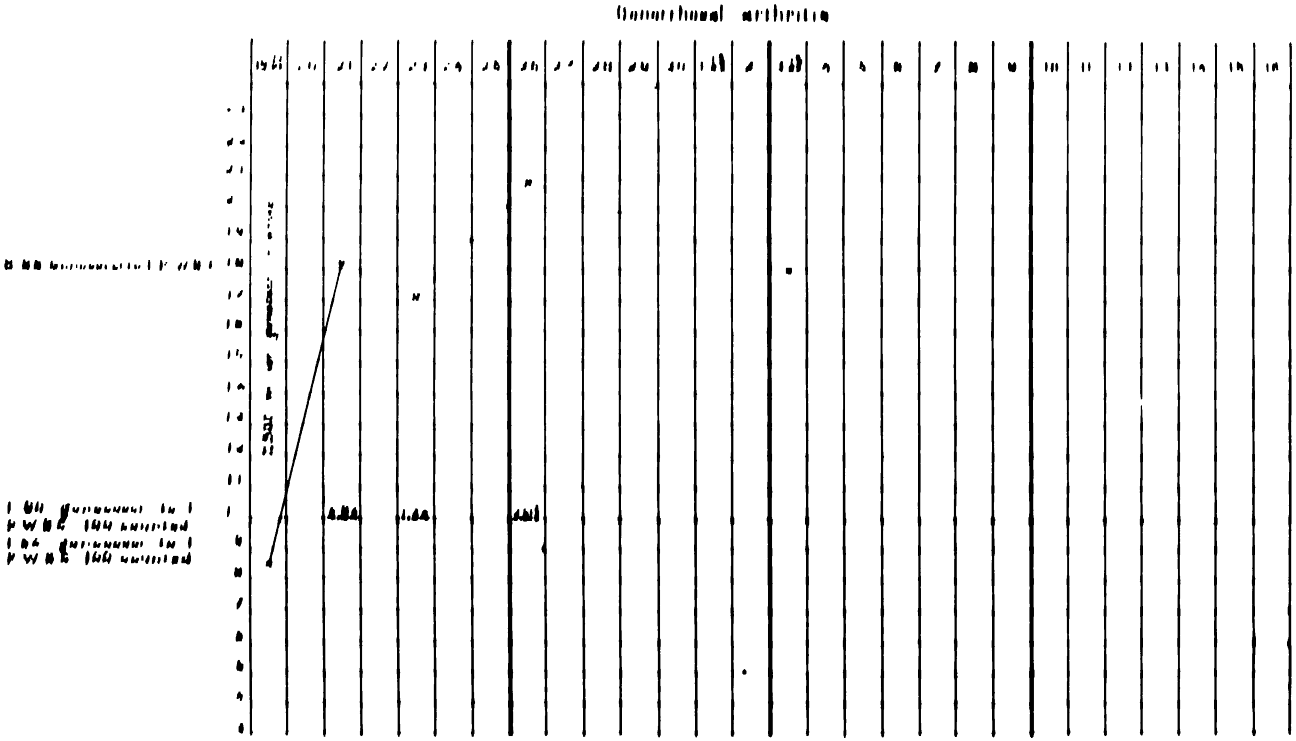
CHART I.



10 11 08 opsonic index .88; 21 11 08 opsonic index 1.83; 23 11 08 opsonic index 1.78; 28 11 08 opsonic index 0.80; 3 12 08 opsonic index 1.0.

SANITARY CONDITIONS AND NEEDS IN PROVINCIAL TOWNS.[1]

By THOMAS W. JACKSON.[2]

The circumstance of continued residence in provincial towns, (where the opportunities for observation of social and sanitary conditions surpass those for studies purely medical), is the principal reason for my choice of this topic. Some members of the Philippine Islands Medical Association have spent a good portion of the past ten years in these Islands, others have had interrupted residence, and some have returned after five years' absence or longer in America. To this last class, at least, a comparison of conditions then and now is interesting.

In Manila, at every hand, striking changes in methods and facilities for transportation, communication, procuring of food, recreation, illumination, and external conditions affecting the comfort and safety of living for Americans are in evidence. Great improvement in highways, buildings, sewers, hospitals, schools and churches, and bettered conditions as to the control of epidemic diseases are notable.

A splendid Bureau of Science and a Medical College have been established. Exhaustive studies of tropic diseases have been undertaken and important facts concerning their causation have been discovered. In a word, great things have been wrought.

Both in and out of Manila, American soldiers and sailors are so safeguarded that the morbidity rate for the Islands is slightly less than that for the United States. Conditions are less favorable for Americans outside of garrisons, but with due attention to hygienic law and the observance of well-known precautions against infection, reasonable health may be maintained by all. The relative infrequency with which Americans have suffered from epidemic plagues, such as cholera, emphasize this contention.

The Director of Health for the Islands stated in the annual report for 1906 that "each succeeding year of experience in health work shows that the white man's chances of contracting disease in the Philippine Islands are less than in the United States." He also shows statistically that for the year 1906 the death rate, including those who died after returning to America, was not higher than in the most salubrious communities in the United States. He further states that "in no country in the world has the Government done more for the protection of its employees." Granting the correctness of these statements we may dismiss the white man from our consideration and turn our attention to conditions among Filipinos in the provinces. Inasmuch as 95 per cent of the Filipino people live outside of the city of Manila we may fairly take conditions outside of that city as an index of our success or failure in hygienic education at the end of nine years of American occupation.

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[1] Read at the Fifth Annual Meeting of the Philippine Islands Medical Association, Manila, February 29, 1908.

[2] First lieutenant, Medical Reserve Corps, Fort William McKinley.

Let us consider these conditions briefly. It would be unfair to inquire whether the improved conditions just recited for Manila obtain likewise in provincial towns. It is fair, however, to inquire in what respect sanitary conditions in provincial towns are better than they were at the time that American civil government was instituted in these Islands. I have lived in native houses in provincial towns for the past year, closely surrounded by Filipino neighbors and by day and night I have observed their customs and habits. Under the circumstances, indeed, it would be impossible to avoid an intimate knowledge of their manner of life. In 1901 and 1902 I had a similar opportunity and I therefore feel that I am qualified to make comparisons. The habits, customs, and manners of the people are sufficiently well known to most of the members of the Association and I have reason to believe that the conditions I have observed are neither better nor worse than those in the average provincial town. Putting aside matters which are purely æsthetic and fully recognizing the great progress made by the government in its efforts to provide for the people the things which make for peace and contentment, I am of the opinion that our efforts at sanitary education, if they have not failed completely, have been far from successful.

Accepting the testimony of my eyes I am forced to believe that in provincial towns conditions are practically as they were seven years ago, as regards such personal habits as defecation, urination, expectoration, and eating with the fingers. In less individual matters, affecting the community rather than the family, such as the condition of the market places, the contamination of foods by insects and animals and the disposal of garbage and other wastes, the improvement is inappreciable. There is sufficient improvement for remark in the single matter of relative tidiness of streets and dooryards. Even in this particular, which is cosmetic rather than vital from a sanitary viewpoint, one can point to little more than the disappearance of carabao wallows. It is true that in every town of any size there are people of comparative wealth and relative intelligence and education. Some of them have been educated in schools of our establishing. These people exhibit cleanliness of person and clothing, eat at tables with spoons and forks and give evidence of a desire for better things for their countrymen. This part of the population as compared with the whole, however, is inconsiderable and it must be admitted that even in the case of the wealthy and intelligent, sanitary matters which really count are quite neglected.

Let us take for example a certain provincial capital less than one hundred miles from Manila. The population is between 8,000 and 10,000 people. The provincial government offices, prison, and high school are located here and the governor and members of the provincial board reside in the town. The town is situated upon the bank of a river which serves as a sewer and water supply, as a universal bath-tub for people and animals, and as a wash tub for the clothing of 10,000 people. Passing through the streets we encounter chickens, ducks, goats, half-starved dogs and unnumbered pigs, many of them with decorations of human fæces on their heads and backs, foraging for garbage or the droppings from passing horses and carabaos. Markets and *tiendas* expose their wares of fruits, cooked rice, fresh meats, fish, vegetables and crude sugar to the clouds of dust in the streets and flies swarm in thousands over the sticky sugar and bloody meats. Dogs and cats walk over the exposed vegetables and natives, with fingers whose condition may be imagined rather than described, handle the food *ad libitum*. Screens against flies are everywhere absent. Defecation is performed in public at all times upon the streets and river banks. With one exception, the water-closets in all homes but those of the Americans are of the pig-flushing variety.

Stagnant pools of waste water are found beneath many houses, serving as pig-wallows or as mosquito-breeding places. The ubiquitous and iniquitous pig feeds upon human excrement and in the end serves as food for the people. Nudity, under the law, is a punishable offense, but boys and girls of the age of pubescence parade the streets, practically naked, before the eyes of American women and children. In this town there are 27 Americans variously connected with the Civil Government, Educational Department, Constabulary, and Army. There is annually expended for salaries of American teachers stationed here (most of them in the provincial high shool) more than 20,000 pesos, Philippine currency, while for practical sanitation, exclusive of extraordinary expenditures for the suppression of epidemic diseases, I am unable to learn of any outlay. A native physician, formerly employed as municipal physician at 30 pesos per month, is now filling the office of district health officer. He draws a salary of 200 pesos per month. He is the sole official representative of sanitation and he is absolutely inactive so far as local conditions are concerned. There is no municipal physician.

It is interesting to know that upon the municipal statute books of this particular town there are ordinances, with penalties for their violation, covering practically all of the abuses which I have named. These ordinances are absolutely dead letters. They are doubtless unknown to a large part of the populace. They provide for garbage collection and disposal and for a sanitary cart for the house-to-house collection of excreta and other wastes. They prohibit the running at large of pigs and other domestic animals and prescribe penalties for the violation of these provisions. They provide for the screening of foods in market places and for inspection and policing. In short, they provide for the maintenance of decent conditions, which is probably as much as we can reasonably expect in this country.

This recital is not made to excite commiseration for the Americans who by force of circumstances are obliged to live in these towns and endure these conditions; neither is it in any sense a complaint against the constituted Health Department of these Islands. If I sought to excite sympathy for the Americans I would relate conditions as they exist in another large town in the same province, where matters are worse than I have described them. As for the Public Health Department we can not overlook the tremendous work it is doing and has accomplished, especially in the sanitation of Manila, the establishing of vital statistical records, charity hospitals, the vaccination of the people, the control of epidemics, the segregation and colonization of lepers, and best of all the enactment of laws.

It is rather on behalf of the Filipinos themselves that I have described conditions as they are. The question which propounds itself is this: "Are we doing less than our duty to the Filipino people in this matter?" I fear that we are. Whether we agree with the doctrine that the United States is exercising a temporary control of the Islands preparatory to entire withdrawal therefrom, or whether we consider the Islands as colonial possessions, it must be admitted that at present the United States Government is actually in possession and control. As candid medical men and good Americans we recognize, as our duty, the obligation to promote health conditions in these Islands to our utmost. This obligation is not contingent upon the wishes of the Filipinos. We hear a great deal these days about altruistic government. In what way can real altruism be better shown than by requiring the observance of hygienic law?

In the last annual report of the Bureau of Health for the Islands attention is called to "the comparative freedom from disease which residents of the Philippine Islands who are willing to follow the few simple rules recommended by the Bureau of Health enjoy". In this statement lies the explanation of the situation. Residents of the Islands are "permitted a choice" as to whether or not they will observe hygienic laws, the violation of which affects not only themselves, but their fellow-men. So long as this is our policy we can hope for little improvement. Surely we can not hold the Health Department accountable. The Bureau must reflect the policy of the Government. It has been stated that "the mere suggestion of interfering with the home life of the people would cause storms of protest."

As earnest men, seeking as a common end the betterment of humanity in these Islands, we can afford to consider well it seems to me whether a storm of protest should stand in the way of decency and the fulfillment of a pledge to the civilized world to lift these people from all that is destructive and degrading.

What are the probabilities of opposition on the part of the Filipinos to the enforcement of sanitary laws such as have been referred to in this paper? Doubtless there would be both silent and public opposition, but I do not believe that it could possibly attain to dangerous proportions or cause lasting disaffection. Witness the acquiescence of the people following the gambling laws and the sedition and flag laws. Where has there been effective or successful opposition to the enforcement of cholera regulation or the segregation of lepers? The present may well be called a period of the Reign of Law, and it seems to me that the present is the opportune time for sanitary reform. Moreover, there is no doubt that the educated class of Filipinos would conform to the laws and support them with influence, when once apprised of their importance, the necessity for compliance, and the unavoidable penalties of noncompliance. That the liberties of the people would be affected by such reform is not to be seriously contended.

When the provincial boards of health were abolished in 1906 there were vested in the district health officer the following duties and powers:

> General supervision and control over health and sanitary works and over municipal boards of health in the district; power to institute proceedings to abate nuisances and to prosecute violations of the law; to recommend to the Director of Health sanitary regulations for prisons, schools, and institutions; to make internal quarantine regulations; to attend all persons entitled to free medical attendance, and to compile statistics. District health officers are authorized to require owners, agents, and occupants of buildings to maintain sanitary conditions and are themselves required to call upon *presidentes* to enforce municipal laws.

Consider the very great possibilities of sanitary accomplishment under this law, if all district health officers were competent, energetic, fearless men, unhampered by political complications. No argument is needed to show that under existing conditions in the Islands few Filipinos in the provincial towns are qualified for these positions. Political intrigues and the fear of offending powerful interests disqualify many of those who have the necessary executive or professional attainments. To look for relief in sanitary matters through the pressure of native public sentiment created by the advice of Filipino physicians, as has been suggested, is chimerical I fear. Likewise, the introduction of sanitary teachings into the home through the school children must be a slow and tedious process, unlikely to produce results within a generation. I have heretofore contended that the teaching of hygienic principles is a necessary and preliminary foundation for any material development of the people of the Philippines, and I am more than ever convinced that the enforced observance of basic hygienic laws must prevail before progress worthy of the name will be made.

The teaching of hygiene and sanitation has a place in the scheme of public education for the Islands and doubtless much good is accomplished thereby. The matter is a delicate one for the average teacher and is not given the prominence in the course, I suspect, that it deserves. In November last, at the invitation of the principal in charge, I gave two lectures to the pupils of the provincial normal school in session in one of the provincial capitals. These students were advanced pupils and native teachers of the primary schools and numbered about two hundred. Judging from the number of questions propounded after the lectures were over there seemed to be shown an encouraging interest, but an extremely elementary knowledge.

Doubtless these conditions will be overcome in due time. In the mean time we should try the effect of the enforcement of sanitary law.

I have not considered it necessary to attempt to show by argument, or by the citation of statistics, the relationship between filth and disease. The fact that the public health is indirectly affected by the insanitary practices of the people is well understood by a body of men of the character of this Medical Association. It would be difficult to think of many serious tropical diseases which may not be disseminated by some one or more of the practices which prevail here. Neither have I considered it necessary to discuss the view, somewhat widely held, that the scavenger pig is a blessing in disguise. We should insist at all times that he has no place among the sanitary forces of the Philippine Islands. Not only is he offensive from an æsthetic point of view, but he is entirely inefficient as an animate crematory or germ converter. That pathogenic bacteria and protozoa are rendered benign by a trip through the intestinal canal of a pig is an assumption absolutely without warrant.

As cited by the Director of Health, the pollution of streams is without doubt one of the greatest factors of disease production in these Islands and it is gratifying to read in the last annual report of the Health Bureau of a comprehensive plan to remedy in good time this most serious condition, involving as it does financial and engineering problems of magnitude. For the present, greater attention should be devoted to the matters of soil and food pollution which, it is believed by many, will prove to be nearly as great sources of disease as water pollution. Compared with the task of furnishing a pure water supply these problems should be easily solved. Apparently we already have sufficient law. It is not to be expected that miracles will be wrought by its enforcement, but conditions can certainly be bettered. The Director of Health has stated that "with very little cost the hygiene of domestic life could be very much improved." I am of the opinion that the same statement holds good for municipal hygiene and doubtless we all agree with him that "efforts along this line would be well rewarded by the greatly decreased mortality which would be sure to result."

It seems to me that meetings of the character of this Medical Association are proper places for the discussion of questions of hygiene and sanitation. We feast intellectually upon masterly papers which present the purely scientific side of our profession. New and attractive vistas of possibility are unrolled before us, as suggestive hypotheses in explanation of problems hitherto baffling are presented.

It is neither belittling nor damaging to our dignity to consider the simpler questions of sanitation in the home and in the community. In so doing one is often obliged to pronounce opinions and to offer friendly criticisms which are apt to be misinterpreted as malevolent.

In conclusion I wish to state that I have abiding confidence in the motives, plans, and ultimate success of the Philippine Government in the great sanitary battle in which it is engaged. I believe that the phase of the problem which I have attempted to present is an important detail, worthy of attention now, but I am not unmindful of other phases nor of the magnitude of the work in hand and results already achieved.

EDITORIAL.

DISCUSSION OF THE PAPER BY DR. THOMAS W. JACKSON.

Dr. Victor G. Heiser, Director of the Bureau of Health of the Insular Government and professor of hygiene in the Philippine Medical School: I feel grateful to Dr. Jackson for presenting this paper because it gives me an opportunity to reply to a great many criticisms as to the manner in which local hygienic measures are carried out. The point of view makes a good deal of difference. Some persons think that it would be easy to remedy these unfortunate conditions. Those of us who have had most experience in dealing with them know that this is not true. Hygienic methods have passed beyond the stage where the cleaning up of backyards, or the penning up of pigs are considered matters of fundamental importance.

It is not well for a health officer to occupy himself too much with these matters. His legitimate work is much deeper and is more far-reaching in its effects. It is probable that we could have the hogs kept in their proper places, but after all such measures would result in raising a strong opposition which might interfere with the more important measures which we have in view.

We do not at present attempt to interfere to any considerable extent with the personal habits of the residents of these Islands in spite of the fact that some of these habits are very unsanitary, but are occupying ourselves with matters of greater importance. We are attempting to vaccinate the entire population against smallpox and are bringing about very gratifying results. In the provinces immediately adjacent to Manila the annual deaths from smallpox until very recently amounted to at least 6,000, but last year there was not a single death in these provinces from this disease.

We have been urging the boring of artesian wells, particularly in towns where the water supply has been found to be especially bad. We find that the people are glad to utilize the comparatively pure artesian well water for drinking purposes, instead of the contaminated water from shallow wells and open springs and streams which they formerly drank. We find, furthermore, that in a number of towns where artesian wells have been bored the death rate has fallen from 30 to 50 per cent, and I contend that this is a much more important reform than would be the putting of all the hogs in pens.

My attitude is that the people should be left alone so far as concerns matters of minor importance and that we should concentrate our efforts on the obtaining of large results from the really fundamental measures we now have under way. The people have now begun to be influenced by those of their number who are educated in hygiene. We do not need to go back farther than 1902 and 1903 in order to note a striking change. At that time the method universally employed in combating cholera was to hold religious processions, but we have patiently instructed the people in hygiene and since 1905 religious processions have been regarded as almost a negligible factor in preventing the spread of this disease. This result is one of very great importance. We should attempt to make effective measures which will reach and influence thousands rather than those which will reach tens.

Sir Allan Perry, Principal Civil Medical Officer, Ceylon: I wish to congratulate the gentleman on his paper. He naturally expects conditions to improve, and he regrets that after an absence of some years he comes back and finds them the same as when he left. My observations have been made in places that have been under the control of our government for one hundred years, and the conditions we encountered are very much the same there as they are here. It seems to me that he desires to go too fast. We can not alter the condition of the people simply by making laws. They will not observe them, but it is to be hoped that by education in modern sanitary measures they can be persuaded to bring about improvements of themselves. One more thing has struck me, and that is the influence of heredity on the condition of a people new to modern ideas.

Dean C. Worcester, Secretary of the Interior and Member of the Philippine Commission, Manila: There is one practical query which suggests itself in connection with Dr. Jackson's recommendation that we now proceed to carry out sanitary regulations by force. Can this be done in actual practice, or is the program which he outlines too ambitious?

A short time ago there was submitted to me a remarkable series of health ordinances intended to apply to the Igorots of the Province of Benguet. They were drawn up by an American health officer residing at Baguio who had obtained copies of the sanitary ordinances of the city of Manila and had persuaded the Igorot township council of Baguio to pass many of the most important of them and was attempting to enforce them among the wild people.

One must know these people in order fully to appreciate the absurdity of such an attempt. The ordinances contain specific provisions as to the construction and location of water-closets, when in point of fact no Igorot in Benguet Province has such a thing, if indeed there is any one of them who has ever heard of their existence. If an Igorot desired to dig a well it was made incumbent upon him to send to Manila and get the Director of Health to approve the site selected. It was necessary for me to disapprove this whole series and to bring about the enactment in the form of ordinances of a few simple hygienic rules suited to the conditions and to the intelligence of these primitive people.

Referring to Dr. Jackson's statements relative to the opposition likely to be encountered in carrying out the program which he outlines, permit me to suggest that two kinds of opposition are certain to be encountered in this country, namely, active opposition and passive opposition. The first has not been lacking and Dr. Jackson has evidently never heard of certain facts which stick in my memory.

Not only have we had the efforts of efficient men rendered utterly futile by the active opposition of demagogues and politicians who have stirred up the people, but we have had sanitary inspectors murdered outright. While we are doubtless entirely capable with the armed force at our disposal of sitting on the lid no matter how much political fermentation the agitators may succeed in stimulating, it is, I am certain, far more easy to *persuade* people such as these with whom we are dealing in these Islands, to observe sanitary ordinances, than it is to compel them to do so, and disturbances of public order are not helpful if they can be avoided.

But however serious may be the results of active opposition the difficulties and obstacles created by the *passive* opposition of an Oriental people like the Filipinos are far more formidable. I am sure that every one of us who has encountered this opposition has an especially keen appreciation of Kipling's description of the sad fate of the man "who tried to hustle the East."

Dr. Jackson states that we have ordinances to cover everything, but that they are not enforced. I say that at the present time it is impossible to enforce all of them unless you pin them to the backs of the people with the bayonet, and to attempt to inaugurate such a policy would be foolhardy in the extreme.

Our general sanitary measures for the suppresion of smallpox, cholera and leprosy appeal strongly to the people. They can see and appreciate what we are doing along this line and we are gradually gaining their confidence and support.

While we have a large body of Filipino physicians in Manila who understand how to deal with individual cases of illness, these men have not had any general sanitary training. It was impossible for them to get it in Spanish times and we ought not to expect them to have it now. Until we have in these Islands a very much larger number of well-trained men who know the customs of the people and who can persuade them to adopt sanitary reforms without raising needless opposition, the fundamental laws of sanitation will continue to be violated. It takes men of the right sort to do these things, but suitable men are so scare at present that we can not fill our vacant positions. How many men would it take to carry out Dr. Jackson's program of enforcing sanitary laws and ordinances by force in one such town as San Fernando, La Union, with its 64 separate barrios or villages?

We should not forget that even in the United States sanitary conditions which leave much to be desired are only too common. How then can we expect immediately to remedy such conditions here? It is so easy to pass a good law and then to imagine that all difficulties have been met and solved. It would, I am sure, be easy to secure a majority vote of the Philippine Legislature in favor of a law providing for the entry into the kingdom of heaven of all of the inhabitants of the Philippine Islands, but I fear that the passage of such an act would work no material change in the present condition of public morals.

In actual practice we find it necessary to advance little by little, feeling our way as we go. The attempt to enforce sanitary measures which are scientifically correct has not infrequently done serious harm in the past. The mistakes of this kind made during the cholera epidemic of 1902 are still green in the memories of many of us. We succeeded in arousing hostility and opposition which for some time went far toward nullifying our work. In drafting and enacting legislation we must seek to get measures which will bring results rather than those which look well on paper but can not be enforced in actual practice.

We are rapidly reducing the number of victims of leprosy and smallpox. We have succeeded in completely eliminating bubonic plague. We are confronted by the grave problems presented by the prevalence of tuberculosis and of hookworm disease. In my opinion we should concentrate our efforts for the present upon combating these diseases, which cause such a shocking mortality. After we have eliminated them we can turn our attention to ordinances dealing with less important matters. I hope for the time when a comprehensive series of health ordinances can be enforced throughout these Islands as I hope for the millennium, but it is my opinion that one is about as distant as the other.

Dr. Henry J. Nichols, first lieutenant, Medical Corps, United States Army: Dr. Jackson has had a considerable experience in the Philippine Islands. He has been on the ground and has personally seen many things. His views are not Quixotic, and I fully agree with him in certain of his suggestions. Manila has been made a beautiful spot, and those of us who have been in the provinces and have seen the lamentable lack of sanitary measures, find that a great discrepancy exists between Manila and the provinces, not only as relates to disregard of the law, but also to a disregard of personal habits relating to cleanliness.

Dr. N. M. Saleeby, superintendent of the University Hospital, Manila: There is left but little for me to say. I have had experience in the provinces. I served on provincial councils, and had a chance to look into these matters. I have seen small towns where a change of officials made marvellous improvement in the conditions, and I think the whole is a matter of local government. It will take a considerable time before we can get these matters straightened out, but I want simply to emphasize the fact that much of what we call insanitary conditions in the provinces can be laid to the door of the municipalities.

Dr. Henry Fraser, director of the Institute for Medical Research, Kaula Lumpur, F. M. S.: The country which we have occupied for thirty years, The Federated Malay States, is healthful and attention is, of course, directed to the water supply, and not to the particular factors in life. The main work is done in the outlying districts.

As regards our efforts in sanitation, such as the combating of malaria, the government has expended large sums of money which are now bringing about good results. In reference to the education of the laity in combating disease, instructions are given in simple language to the school children and by them given to their parents. This method has proved satisfactory.

Dr. Jackson: I am sorry that my paper has been taken as a reflection on the health authorities and the Government. I believe in the Government of the Philippine Islands, but on the other hand I think the individual has a right to his views, and I only expressed views that I have observed in conversation with other Americans. My own personal view, which is all I put forward here, is that the native of the Philippines has a great respect for law, and I believe these laws as they now exist can be enforced without expense, and I believe with Dr. Saleeby that the trouble lies with the local authorities.

I do not hesitate to say that the conditions as they are now can, within a very few months, without the expenditure of very much money, be remedied and the ordinances relating to sanitation be enforced. I know the Filipino people well enough to know that if the leading men of the towns were instructed and told what to do, they would help us. If the enforcement of these laws could be placed upon the health officers of the provinces and at the expense of their positions, I think that the laws would be obeyed in six months' time. I do not lay much value on the sweeping up of towns, and in this respect I have nothing to offer to the Health Department or to the Government, but I think what we need is criticism. My criticisms in this matter are entirely friendly and I am sorry that anyone should take any other view of it.

Dean C. Worcester: I regret that Dr. Jackson should feel that anyone connected with the Bureau of Health would object to honest criticism. He certainly ought to know by this time that it has become impossible to hurt the feelings of Dr. Heiser or of myself. We have developed hides as thick as those of a pair of rhinoceri and the darts of the enemy produce not the slightest impression upon them.

But Dr. Jackson must not expect to make criticisms without drawing our fire in return. I understand this to be a fitting occasion for the free interchange of ideas. I spoke somewhat hastily, as I had a good deal to say and knew that Dr. Musgrave was holding the watch on me and might call time at any moment and I perhaps failed to make my meaning entirely clear. I do not object to anything that Dr. Jackson has said. We are only too well aware of the fact that we have made mistakes in the past and are more than glad to have any well-meant suggestions as to how we may do better in the future, but in closing permit me to say that any one who talks of bringing about a general enforcement of sanitary regulations throughout these Islands within a period of a few months has a very imperfect conception of the problem with which we are confronted. We are doing all we can with the money and men at our disposal. Certainly many of the members of this association know that the death roll of Americans in these Islands bears the name of more than one faithful and efficient sanitary officer who has killed himself with overwork.

I insist that it will take a much larger body of men than we now have, as well as enormously increased appropriations for health purposes to bring about such conditions as Dr. Jackson believes could be readily secured and it should be borne in mind that I am not a pessimist on this subject.

I remember only too well that at the inauguration of our sanitary work here I was called insane because I believed that we could hope to accomplish certain things which have now been done, and I wish that it might prove true that Dr. Jackson is right and that I am wrong. The picture which Dr. Jackson has painted of conditions in our provinces and municipalities is absolutely true to life. The practical question is "what are we going to do about it"? We are not at all sensitive over having our past shortcomings criticised and what we *particularly* desire is a practical illustration of how it ought to be done. Nothing would afford me greater pleasure than to approve the appointment of Dr. Jackson as a district health officer and to afford him all possible support in an effort to realize in only a single health district his expectations as to what may be done.

REVIEW.

Clinical Bacteriology and Hæmatology for Practitioners. By W. D'Este Emery, M. D., B. Sc. Lond. Third edition. Cloth. Pp. xxxiv+252. Price $2 net. Philadelphia: P. Blakiston's Son & Co., 1908.

The author has endeavored to bring into the narrow confines of 250 pages those fundamental facts of bacteriology and hæmatology which are needed by a physician who does not have access to a good laboratory. The subject matter is presented in a remarkably clear manner and the arrangement is such that for any particular examination a description of the necessary apparatus and method of procedure is found in full, so that the reader does not have to refer to various portions of the book to obtain the desired information. This entails a certain amount of repetition, but greatly increases the practical value of the book.

Since bacteriology has been taught in almost all medical schools for a number of years past, the younger generation of physicians will find much here that would seem superfluous, along with many valuable suggestions as to the clinical applications of his bacteriological knowledge. The book is written, however, primarily for the older generation who did not have any bacteriological training and for them it will prove to be entirely satisfactory.

Only very few errors have crept into the work. One misses bile media in the blood culture of typhoid and V. Pirquet's cutaneous reaction for tuberculosis. Owing to the entirely doubtful value of opsonic index determinations, it would seem that too much space is given to their discussion.

The section on hæmotology is taken up mainly with the estimation of the amount of hæmoglobin, red and white cell counts, and the differential leucocyte count.

The accompanying plates are very satisfactory and add materially to the usefulness of the book.

The work as a whole is to be commended for its clearness and the attention that has been given to details of practical value to the practitioner.

Oscar Teague.

The Philippine Agricultural Review

A MONTHLY ILLUSTRATED REVIEW PRINTED IN ENGLISH AND SPANISH AND PUBLISHED BY THE BUREAU OF AGRICULTURE FOR THE PHILIPPINE ISLANDS.

Edited by G. E. NESOM, Director of Agriculture.

The Philippine Agricultural Review, a newly established publication of the Bureau of Agriculture, will take the place of the press bulletins heretofore issued by that Bureau. It will not be a technical journal, but rather a popular serial publication on general agriculture. The primary object of the *Review* is to furnish an educational means of reaching the people of the Philippine Islands with the work of the Bureau of Agriculture.

The first number of the *Review* is devoted entirely to the annual report of the Bureau of Agriculture for the past fiscal year. This report is so published for the purpose of giving to persons interested in Philippine agriculture a comprehensive idea of the organization, scope, and extent of the work of that Bureau. Succeeding numbers will contain reports on agricultural conditions in different parts of the Philippine Islands, articles on tropical agriculture, and other material of interest to readers of agricultural literature.

Volume I, beginning January, 1908, will be issued monthly, and will be circulated free of charge in the Philippine Islands. A limited number of copies will be sent free to foreign workers along agricultural lines in recognition of valuable services rendered the Bureau of Agriculture. Should there appear to be a demand for regular foreign subscriptions, arrangements will be perfected later for furnishing them at a reasonable price.

Persons receiving the Philippine Agricultural Review are invited to submit material for publication. Any reports, articles, or notes on agricultural subjects will receive careful consideration and, as far as practicable, will be published.

Applicants for the *Review* should state whether the English or the Spanish edition is desired. Address all communications relative to this publication to the DIRECTOR OF THE BUREAU OF AGRICULTURE, MANILA, P. I.

THE PHILIPPINE

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B. MEDICAL SCIENCES

VOL. III DECEMBER, 1908. No. 6

STREPTOTHRICOSIS WITH SPECIAL REFERENCE TO THE ETIOLOGY AND CLASSIFICATION OF MYCETOMA.[1]

By W. E. MUSGRAVE and M. T. CLEGG, with
a bibliography by MARY POLK.
(From the Biological Laboratory and the Library, Bureau of Science, Manila, P. I.

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[1] To be read in abstract at the Bombay Medical Congress, February 23, 1909.

INTRODUCTION.

Before entering on a study of the etiology of mycetoma, it is necessary to define the disease. This is exceedingly difficult, either from a clinical or an etiologic standpoint.

Formerly the diagnosis was based upon a clinical picture the essentials of which were a chronically enlarged foot with sinusses from which were discharged small granules of various colors and consistency, accompanied by a peculiar, oily degeneration of the tissues. Further classification was made principally upon the color of the granules; black, ochroid, white, red and mixed varieties being recognized. However, when bacteriologic studies began to show the multiplicity of the organisms concerned in the production of Madura foot it became necessary either to consider it a clinical entity of multiple etiology or to attempt an etiologic classification. This was made still more imperative by the discovery that the organisms causing this symptom complex were found also producing lesions in other parts of the body. A number of authors have continued to use a clinical classification, while others have attempted to give one based upon etiologic findings. The result is great confusion in the nomenclature of the disease.

As a prerequisite to an etiologic classification and definition of mycetoma it is necessary first to know and to be able to classify the etiologic factors concerned. So far this has not been done satisfactorily. The botanists are hopelessly confused in their grouping of the organisms and in consequence medical men have been unable properly to identify them. In the first place, authorities differ as to where the group of organisms belongs in the vegetable kingdom, some placing it among the bacteria and others higher up among the fungi. Practically all the latest writers upon the subject agree as to the great similarity between the various species of these organisms and the majority have placed them as species of a single genus, or as parts of two or even three closely allied genera. In order to establish a uniform and clear conception, and after carefully studying all phases of the question we have decided tentatively to accept *Streptothrix* Cohn 1875 as the generic name of the group of organisms under discussion.

The result of this decision is that the other names given to the tentative genus, such as *Actinomyces, Nocardia, Oöspora,* etc., become synonyms, the disease streptothricosis being limited to infection with parasites properly belonging to the genus, the various species of which will be considered presently.

Adopting such an interpretation, we have a fairly definite group of organisms with reasonably uniform pathologic and clinical manifestations, connected with other groups of closely related organisms giving somewhat similar manifestations. For example, the *Oïdia* or *Blastomyces* on the one hand and the tubercle bacilli on the other, may somewhat closely resemble the *Streptothricæ* in their action in certain parts of the body.

Mycetoma may be defined and classified in one of three ways, if *Streptothrix* is accepted as the most available generic name.

(1) It may be considered as a clinical disease of multiple etiology (which may or may not be limited to *Streptothrix* infections; (2) the term may appropriately be made synonymous with streptothricosis, actinomycosis, nocardiosis, etc.; (3) it may be made a clinical type (foot infection) by a *Streptothrix* (*Actinomyces* or *Nocardia*). Each of these classifications has something in its favor and also may be criticised.

The first would make diagnosis easy, for all forms of foot enlargement giving certain clinical manifestations regardless of the etiology, known or unknown, might be included, but it is open to the objection of not being definite and does not conform to our present methods of etiologic classification.

The second method has much in its favor and is practically adopted by Manson. The objections to it are that it adds a new significance to a term which does not clearly express the conditions and also adds a further synonym to a group of infections already rendered confusing by the number of its synonyms. The difficulty can more satisfactorily be met by the third method.

We have therefore decided to follow the third classification making mycetoma a *clinical* type or variety of streptothricosis—*Streptothricosis pedis*—and to define it as follows:

A disease consisting of a *Streptothrix* infection of the foot (*Streptothricosis pedis, Actinomycosis pedis*), characterized by a chronic course, swelling and deformity of the part, a peculiar, oily degeneration of the tissues with cavity and sinus formations and the discharge through the fistulous openings of mycotic aggregations containing the microörganisms.

Mycetoma, with this definition, becomes so intimate a part of streptothricosis that a balanced conception of it can only be obtained by a study of the whole subject of streptothricosis and a classification of the organisms concerned.

For this reason, the scope of this paper has been enlarged to include a discussion in two parts of the whole subject of *Streptothrix* or *Nocarida* infections.

PART I.

ORIGINAL WORK.

MATERIAL.

The material for this paper consists of the following cultures:

1. *S. freeri* Musgrave & Clegg, *This Journal* Sec. B. (1907), 2, 477.

2. *S. maduræ* Vincent. (This culture was sent to us by Professor Foulerton who writes as follows concerning it: "This culture has been in my hands for the last ten years; it corresponds with Vincent's description of his organism, and

is apparently of the same stock as that from which all the cultures in the London laboratories are derived.")

3. *S. maduræ* Vincent. (This culture was sent to us by Professor Binot of the Pasteur Institute in Paris.)

4. *S. maduræ* Vincent. (This organism was isolated by Dr. R. P. Strong from a case of the pink variety of mycetoma in India, and the culture has been given by him to us, for study.

5. *Streptothrix* of human actinomyces. (From Binot of the Pasteur Institute in Paris.)

6. *Streptothrix* of *"farcin de boeuf"* "A". (From the late Professor Nocard through Binot.)

7. *S. nocardii.* (From Foulerton who writes that "this culture was given to me by Nocard some six years ago.")

8. *S. eppingeri* "A".

9. *S. eppingeri* "B". (Both of these cultures are from Foulerton who writes as follows: "'A' is a descendant of what I believe to have been Eppinger's original culture, 'B' a culture isolated by myself from a case which has not yet been published in detail. I have examined also a third culture of this species obtained by Dr. McDonald from a third case (*The Scottish Medical and Surgical Journal*, 1904). All three strains evidently belong to the same species."

10. *S. capræ* Silberschmidt. (Received from Professor Silberschmidt of Zürich through Binot.)

11. *S. canis* Levy. (From Professor Levy of Strassburg through Binot.)

12. *S. chalcea* Foulerton. (Received from Foulerton who writes that this is a saprophytic species isolated by him from the air.)

The following cultures have also been received, but failed to develop on transplantation:

S. maduræ Vincent. (Furnished by Professor Vincent of the Val du Grace, Paris.)

S. maduræ. (From Legrain de Bougie through Binot.)

Streptothrix of bovine Actinomyces. (From Binot.)

Streptothrix of *"farcin de boeuf"* "N". (From the late Professor Nocard through Binot.)

Streptothrix of Eppinger ("A") and (Kl). (From Binot.)

Streptothrix of Deci. (From Binot who writes regarding this culture that "it was isolated by Deci in the Argentine Republic from a human case resembling tuberculous meningitis." Binot further states in his letter that all the cultures which he has forwarded to us were received by him directly from their authors).

Streptothrix "32". (Received from Foulerton who writes that this organism was isolated by him from a kidney removed from the living patient by operation; the organism was demonstrable in sections of the kidney and was present in large quantity. It is briefly referred to as *S. hominis III* in the *Lancet* (1906), 1, 970. "This organism resembles closely some of the apparently purely saprophytic species, and the infection in the case was probably primary in the lungs."

Streptothrix isolated from a case of mycetoma by Dr. Chaterjee of India.

Dr. Homer Wright states, in reply to a letter regarding cultures of *Actinomyces* and his *"Hyphomycete,"* that he no longer has cultures of these organisms.

A comparative study under conditions as nearly alike as possible has been made of all these strains, with due consideration of their morphology, biology, and pathogenic character. All of them, to obviate as much as possible any influence of long cultural environment were, where feasible, first passed through animals and the studies then made from the reclaimed cultures taken from the experimental lesions. All the cultural and other biologic properties have so far as we have been able to do so, been studied under the same conditions in regard to media, temperature, and generation from animal lesions. Our results and consequent descriptions show some variation from previous descriptions of some of these organisms, but in general the picture is very much as given by the original authors.

We have failed entirely to obtain a culture of the Wolf and Israel and Wright type of *Actinomyces,* but, because of the great importance of this organism in the discussion, we have, for comparative purposes, taken James Homer Wright's description of it from his classical monograph. We have also failed to secure a definite culture of Bostroem's *Actinomyces,* although the one sent by Professor Binot from the Pasteur Institute is probably of this species. However, in view of a possible mistake we have used both the description given by Bostroem as well as the Pasteur Institute culture in our comparative work. The important characteristics of our cultures are shown in the following descriptions and are summarized in the attached table.

No. 1. *Streptothrix freeri.* This organism was isolated by us from a case of the ochroid variety of mycetoma and has already been fully described (*This Journal, Sec. B* (1907), 2, 477). It is identical with Eppinger's organism which will be discussed subsequently in this paper, and the name given by us in the first publication should fall as a synonym for *S. eppingeri,* the latter having priority. Other described organisms of the group which are probably identical with this are those of Stokes, Aoyama and Miyamoto, MacCallum, Sabrezes and Rivière, and possibly several others.

No. 2. *Streptothrix maduræ.* This organism has been carefully described by Vincent, Foulerton, and others. A summary of its characteristics are given both in the text and table and in our first report and are again shown in the table attached to this paper. Our work with cultures of this species has been in the main confirmatory of the published results of others. We have worked with three cultures received respectively from Foulerton, Binot, and Strong. These strains are identical in every particular except that the one from Binot is less pathogenic for monkeys than either of the other two.

Morphologically this species gives very constant results. The colonies are made up of intertwining, long filaments which may, or may not, be radially placed at the periphery. There is true branching, but no club formation in cultures and none in experimental lesions in monkeys up to fourteen days. The organism takes the usual aniline stains; it is Gram positive, but is neither acid nor alcohol fast.

Culturally it is a facultative aërobe with strong oxygen requirements. It grows well in the incubator and at tropical room temperature. Positive transplants on artificial media are readily made, but some difficulty is often encountered in securing growth from experimental lesions. This difficulty is greatest when large quantities of the material are transferred to the media, probably because of an inhibiting material in the contents of the lesions. This hypothesis is supported by the fact that development is much more easily secured if the granules from the lesions are washed in sterile salt solution before transferring them to artificial media. Growth on satisfactory media becomes apparent in from two to four days; development gradually continues for several weeks, depending somewhat upon the quantity of medium present. The principal characteristics of growth on various types of media are shown in the table.

Pathogenicity: Several monkeys have been successfully infected with the Foulerton and Strong strains of this organism, but results with the one from the Pasteur Institute were all negative. Intra-abdominal inoculation has proved the most satisfactory and under similar conditions the character of the lesions produced varies but little. The lesions consist of nodular, tubercle-like processes in the omentum, abdominal wall, and contiguous tissues. These lesions break down and become surrounded by pockets and channels containing a peculiar, pus-like material in which may be found the microörganisms. (See also animal experiments.)

No. 3. *Streptothrix maduræ.* (Pasteur Institute culture.) This is identical in all essentials with *S. Vincent* except that it is not pathogenic for monkeys. This may be due in part at least to its long cultivation on artificial media.

No. 4. *Streptothrix maduræ.* (Strong's culture.) This organism is identical with Vincent's species and its description has been included in the above.

No. 5. *Streptothrix actinomyces.* This culture was received from Professor Binot of the Pasteur Institute as human *Actinomyces.* It is quite different from the Wright type and it also appears to have slight distinctions from the Bostroem type of *Actinomyces.*

Morphologically it appears in the tissues as a fungus of the ray type, but without clubs in young experimental lesions. In colonies the cultures are dark, almost black in color, are made up of the branching filaments and transformation products, generally with radial arrangement of the terminals at the margins of the colonies.

The organism stains poorly by the usual laboratory methods; it is Gram positive and neither acid nor alcohol fast.

Culturally it is a facultative aërobe and grows on the majority of the usual media. In reclaiming cultures from experimental lesions this organism acts very much like *S. madurae* mentioned above; however, if the colonies are first washed in distilled water and then transplanted to artificial media, growth takes place without difficulty.

This type, like the majority of the species examined, grows better in media containing sugar or glycerine. Pigment is produced in all media and the body of the medium is generally darkened to a considerable extent by the culture. The pigment varies from an ochre-yellow in ordinary agar to a dark, almost black color in glycerine-agar and on potato.

The characteristics on varous media are shown in the table.

Pathogenicity: This species is pathogenic for monkeys by intraperitoneal inoculation. It produces the usual actinomycotic lesion like those seen in the clinical disease in man and animals. The organisms are found in the broken-down mass discharged from the sinusses.

No. 6. *Streptothrix* of *farcin du boeuf* "A," and

No. 7. *Streptothrix nocardii.* These two strains are identical in all essential particulars and may therefore be described together under the correct name of *S. nocardii.*

Nocard's original description of this organism was not very complete, but several other observers have studied his and other strains and a number of good descriptions have been given. Foulerton has devoted careful study to this species and our work is in general confirmatory of his description. We have already noted the principal characteristics of this organism in both the text and table in our first report and a summary is also shown in the table in this one. Photomicrographic illustrations of its appearance in cultures are also submitted.

Morphologically this parasite shows marked variation under different environment. In young cultures and early lesions the hyphal forms are prevalent and quite uniform in appearance, but in older cultures and in colonies from lesions, irregularities are encountered. Coccus and bacillus-like forms predominate and very old cultures may almost have the appearance of mixed culture of bacteria. The filaments may or may not be radially placed at the periphery of the colonies. There is true branching, but no true clubs have been seen in cultures or in experimental lesions up to fifteen days of age. The Gram-Weigert method of staining gives good results and portions acid fast to the Ziehl-Neelsen-Gabbett method of staining are very numerous. The organism is also alcohol fast.

Culturally this species is a facultative aërobe. It grows on the majority of laboratory media at incubator or tropical room temperature; development becomes apparent in from two to four days after inoculation. The difficulty of securing transplants from experimental lesions, mentioned in connection with *S. maduræ* does not obtain with this organism. The principal cultural characteristics on various media are shown in the table and may briefly be summarized as follows:

Small, white, irregular, round, raised, opaque colonies develop on *ordinary agar* after two to three days. Growth is slow and not abundant and no pigment is produced.

Glycerine-agar after three days shows discrete colonies which coalesce later and become heaped up, presenting a moist, meal-like growth. No pigment is produced.

On *potato*, growth appears after 48 hours as a buff-yellow, granular, raised mass without pigmentation or erosion of this medium.

In *bouillon* growth appears after 48 hours as a grayish, flocculent mass at the bottom of the tube, later a few grayish granules appear on the surface of the medium and in some instances "puffball" formations occur at the bottom of the tube. The fluid remains clear.

In *ascitic fluid* a very slight growth slowly develops at the bottom of the tube.

In litmus-milk growth appears only at the bottom of the tube. The milk is not coagulated and its color is not changed.

Pathogenicity: This species is an exquisite tissue parasite for monkeys, and is pathogenic to a less extent for some other animals. Monkeys inoculated in the abdominal cavity and killed after five to fifteen days show characteristic lesions. In the majority of instances the early lesions are tubercle-like formations scattered through the mesentery and other tissues contiguous to the point of inoculation. In some cases pus pockets and channels are formed, surrounded by adhesions and containing granules made up of the microörganisms in the pus-like material. Guinea pigs inoculated in a manner similar to the monkeys give parallel results.

No. 8. *Streptothrix eppingeri* "A," and

No. 9. *S. eppingeri* "B." These strains are identical in all essential particulars and may be described under the correct name of *S. eppingeri*. This is one of the most important species of this group of organisms and has been well described several times. It has been isolated from anatomical lesions of such varying character as those from meningitis, by Eppinger and others, to Madura foot, as has been published in our first report. Foulerton has described this species and we have fully discussed its characteristics in our first report and summarized them in the table in this paper. Our work has demonstrated fully the identity of *S. freeri* with this species and it is probable that several of the varieties described in the literature also must be classified with it. Its characteristics may be summarized as follows:

Morphologically a variety of forms exist varying from small, oval, coccus and bacillus-like bodies, to long branching filaments, depending upon the lesion or the age of the culture and the media used. In tissues the branching filaments are not seen by the ordinary method of staining, the growth occurring as a skein of thread-like filaments and with colony formation. The threads present a beaded appearance by using Gram-Weigert's stain. In cultures portions of the filaments are acid-fast by the Ziehl-Neelsen-Gabbett method, and they are also Gram positive. The entire mass from experimental lesions is often acid-fast.

Culturally the species is a facultative aërobe and grows on the majority of media. Growth becomes apparent on ordinary agar after two days, consisting of a smooth, adherent membrane which at first is porcelain-white, later it develops a delicate, orange-pink color. The medium remains moist and is not colored in its depth.

Glycerine-agar, after about three days, shows a growth consisting of small, whitish colonies, which gradually develop a delicate pink color. Later, as the colonies progress, they become umbilicated and coalesce, forming a heaped-up growth and producing a bright, orange color. The medium becomes slightly darkened.

On *potato* the growth appears after about four days as a granular layer, at first white, later becoming yellowish and gradually assuming a brick-red color. As the colonies develop they become umbilicated then coalesce and finally produce a moist, meal-like growth on the surface of the medium. The colonies can be lifted in heaps from the medium by the platinum loop, and when immersed in salt solution or distilled water readily disintegrate into fine, flat particles which float on the surface.

In *bouillon* growth appears after 48 hours in the form of small, flat particles, which at first are white, but later assume an orange tint on the surface of the medium. As growth progresses, the colonies coalesce and produce a membrane on the surface of the liquid. Portions of this membrane fall to the bottom of the tube.

In *ascitic fluid* a very slight growth occurs after six day's incubation.

Litmus-milk shows growth on the surface of the medium in the form of fine, white particles which in time becomes pink in color. A film is gradually formed on the surface of the milk, which is neither coagulated nor changed in color.

Pathogenicity: The three cultures of this species, including the two strains from Foulerton as well as our own, are pathogenic for monkeys, producing on inoculation characteristic progressive lesions. (See animal experiments.) Typical Madura foot may be produced by inoculation into the feet of monkeys. Subcutaneous inoculation produces abscess-like pockets, containing a thick, viscid pus in which the colonies of the organism may be observed as small, white granules. Intra-abdominal inoculation results in tubercle-like formations with adhesions, breaking down of tissue with abscess and sinus formation. Granules made up of the colonies are present in the abscess contents.

No. 10. *S. capræ.* A study of this species from the culture sent us by Foulerton confirms in general the findings of Silberschmidt and of Foulerton. It shows characteristics which differentiate it specifically from any of the others with which we have worked.

Morphologically this organism more closely resembles the bacteria than the others and in its action on monkeys it also resembles the tubercle bacillus quite closely. The filaments show true branching without club formation and they are shorter than with most of the other species. Bacillus- and coccus-like forms predominate in cultures and are also very prevalent in experimental lesions. It stains by the stronger aniline dyes in a somewhat irregular manner, is Gram positive and largely and strongly acid and alcohol fast.

Culturally it is a facultative aërobe and grows on most of the laboratory media. Growth first becomes apparent in from two to four days and progresses slowly. The cultural characteristics are shown in the accompanying table and need not be repeated here.

Pathogenicity: This organism is pathogenic for monkeys and guinea pigs and by intraperitoneal injection for rabbits. The lesions differ somewhat from some of the other members of the group in that there is much less tendency to suppuration or other form of tissue necrosis. The lesion is essentially a tubercle-like formation which spreads from the point of inoculation by the formation of other small granules. When studied microscopically these lesions resemble the tubercle quite closely, always contain the microörganism and occasionally giant cells are encountered. The tubercle-like granules occasionally break down and form small pockets of thick granular pus-like material, but this is the exception and granules made up of colonies of the parasite have not been encountered as in the other species.

No. 11. *S. canis.* This organism is probably identical with *S. capræ* of Silberschmidt. The only important points of difference in the cultures which we have are shown in the table, and consist principally in the difference in reaction in litmus milk. Morphologically and in its pathogenic action *S. canis* gives very similar results to *S. capræ*. The same tubercle-like lesions are formed in experimental animals and the close similarity in other respects has led to the conclusion that the two belong to a single species.

No. 12. *S. chalcea.* This is a nonpathogenic species reported by Foulerton and carried along in this work principally as a control. It is distinguished specifically from the other species by morphologic and cultural characteristics, and particularly by its being nonpathogenic for monkeys.

ANIMAL EXPERIMENTS.

The following are summaries of our animal experiments. The general results are placed under the discussion of the characteristics of the various species of the microörganisms. A complete summary will be found in the chapter on general discussion and conclusions.

S. nocardi:

Monkey No. 3635, inoculated in the abdominal cavity with one loop of a two months' culture and the animal killed 12 days later. Autopsy shows numerous miliary tubercle-like granules extending over the entire surface of the omentum and mesentery with an occasional suppurative process. The pus when pressed out contains small, yellowish-white granules made up almost entirely of the microörganism.

Monkeys numbered 3722, 3726, 3714 were inoculated in a similar manner to the above. All showed similar lesions with the exception of monkey No. 3722 which gave a negative result.

Guinea pigs and rabbits inoculated in the abdonimal cavity for the greater part developed similar lesions. Intravenous inoculation in rabbits gave negative results.

S. eppingeri:

Monkey No. 3665 was inoculated in the abdominal cavity with one loop of a ten days' culture and the animal was killed thirteen days later. Autopsy shows numerous, tubercle-like granules in the lower portion of the mesentery.

with extensive adhesions of the mesentery to the abdominal wall. On separating the adhesions, or on section through them, numerous sinusses are exposed; these hold a thick, viscid, pus-like substance containing numerous small grayish-white granules composed principally of *Streptothrix*.

Monkeys numbered 3664, 3633, 3622 were inoculated in a similar manner to monkey No. 3665 and the lesions produced were in all essentials similar to those found in that animal.

Foulerton's strain of S. eppingeri.

Monkey No. 3725 was inoculated in the abdominal cavity with one loop of a ten days' culture and the lesions produced are similar to those found in animals inoculated with *S. eppingeri* of the original strain.

S. maduræ.

Monkey No. 3854 was inoculated by opening the abdominal cavity and burying a loop of the material from a two weeks' culture of Strong's strain of the organism. Ten days later the animal presented a distended abdomen with a marked tympanites and was killed on this date. Autopsy shows numerous miliary tubercle-like processes in the omentum and mesentery and adhesions surrounding the inoculated material. The adhesions are easily separated and show small, pinkish-white granules adhering to the mesentery.

Rabbits and guinea pigs inoculated subcutaneously, intravenously, and intraperitoneally with this organism gave negative results.

Monkey No. 3856 was inoculated in the abdominal cavity with one loop of a two weeks' culture of Fullerton's strain of this organism and killed two weeks later. Autopsy shows a small, tumor-like mass made up largely of adhesions confined to the coils of the intestine, omentum, and abdominal wall. On section the tumor shows several small abscesses from which can be expressed a thick pus containing small, white granules composed almost entirely of the organisms. The latter are present in large numbers.

Monkey No. 3724 was inoculated in a manner similar to the above with negative results.

Guinea pig No. 3856 was inoculated into the abdominal cavity with one loop of a two weeks' culture and killed after 10 days. Autopsy shows slight adhesions of the omentum to the abdominal wall and intestine, but no other lesions are present.

Subcutaneous and intravenous inoculations of monkeys, rabbits, and guinea pigs gave negative results in every case.

Monkeys numbered 3719, 3627, 3668 were inoculated with one loop of a two weeks' culture of Vincent's original strain of this organism. The inoculations were made subcutaneously and intraperitoneally and in no instance were progressive lesions produced.

Guinea pigs and rabbits inoculated subcutaneously, intravenously, and by intraperitoneal injections also gave negative results.

Actinomyces (from the Pasteur Institute):

Monkey No. 3864 was inoculated into the abdominal cavity with one loop of a two weeks' culture. The animal died three weeks later. Autopsy shows small abscesses in the abdominal wall at the site of inoculation and numerous miliary, tubercle-like granules in the omentum and mesentery. The pus from the abscesses contains many minute, hard, black granules which by microscopic examination are seen to be made up of a net-work of mycelia and transformation products of the microörganism.

Monkeys numbered 3622 and 3623 were inoculated in a similar manner and presented similar lesions to the above. Intravenous, subcutaneous, and intraperitoneal inoculation of rabbits and guinea pigs gave negative results in each case.

S. capræ:

Monkey No. 3858 was inoculated into the abdominal cavity with one loop of a two weeks' culture and ten days later the animal was killed. Autopsy shows numerous miliary, tubercle-like bodies on the mesentery, diaphragm, and on the surface of the liver. There is slight adhesion of the omentum to the abdominal wall at the site of the inoculation.

Monkey No. 3625 was inoculated into the subcutaneous tissue and into the peritoneal cavity with a suspension of this organism. The animal died three weeks later. Autopsy shows extensive adhesions around the site of inoculation and there is a large abcess in the abdominal wall. On section the abcess contains a heavy, creamy, pus-like material in which are numerous, minute, grayish-white granules. These granules are composed of microörganisms and a pure culture is easily obtained by transplanting the granules to artificial media.

Guinea pig No. 3859 was inoculated in a similar manner as were monkeys numbered 3858 and 3625 and the lesions produced were similar to those described for the monkeys. Intravenous inoculations of rabbits gave negative results in the animals used.

S. canis:

Monkeys numbered 3633 and 3626 were inoculated in the abdominal cavity with one loop of a two weeks' culture and a two months' culture of this organism' respectively, and both animals were killed two weeks later. Autopsy shows slight adhesions near the site of inoculation. The omentum and mesentery are intensely congested and contain numerous miliary, tubercle-like granules.

Monkeys, guinea pigs, and rabbits inoculated subcutaneously showed no progressive lesions at autopsy. Intravenous inoculation of rabbits gave negative results. Intraperitoneal inoculation of guinea pigs in two instances produced lesions similar to those described for intraabdominal inoculations in monkeys.

S. chalcea.

Monkeys, guinea pigs, and rabbits when inoculated subcutaneously and intraperitoneally gave negative results.

LITERATURE.

A review of the literature of this subject may for convenience be divided into two divisions (1) *genus* and (2) *species* determinations.

Several of the generic names which have been introduced are clearly descriptive of organisms belonging to other genera such as *Cladothrix* or *Leptothrix,* and some refer to organisms properly belonging to the classes *Oïdia* or *Bacteria.*

GENUS.

The generic names which appear to have some claim for consideration are as follows:

STREPTOTHRIX.

Corda named this genus, giving, according to Saccardo (Sylloge Fungorum (1886), **4**, 282) the following generic diagnosis:

"Hyphæ fertiles erectæ, virgato-ramosæ, ramis ramulisque spiraliter tortis. Conidia globosa v. ovoidea, in ramulis solitarie acrogena, subinde pleurogena, sessilia v. stipitellata, fusca."

Cohn (Untersuchungen über Bacterien, II.—Beiträge zur Biologie der Pflanzen (1875), **1**, 186) used the name *Streptothrix* in a new sense in describing an organism *Streptothrix fosteri*, which he found in the lachrymal ducts of a patient. The definition for this organism as given by De Toni and Trevisan (Saccardo's Sylloge Fungorum (1889), **8**, 928) is as follows:

"Filamentis tenuissimis, hyalinis, parallele insimul stratiformi-coalitis vel fasciculatis, rectis vel incurvis, sparse irregulariterque ramosis, in fragmenta inaequilia secedentibus."

CLADOTHRIX.

Cohn (*loc. cit.*, 185) under the name *Cladothrix dichotama* described an organism which was later included as the type species of a genus established by Marchand (Botanique cryptogamique, Paris (1883)) of which De Toni and Trevisan (Saccardo, (1889), **8**, 927) give the following generic diagnosis:

"Filamenta basi ab apice superiore distincta, vagina crassa obducta cylindrica, ætate provecta a basi ad apicem magis magisque incrassata, articulata, pseudoramosa. Arthrosporae binae in singulis microbaculis ellipsoideis ortae."

However Mace (*Compt. rend. acad. sci.* (1888), **106**) in a careful study of *Cladothrix dichotoma* Cohn showed that it did not have the supposed property of dichotomous division of the filaments, but that this appearance was simulated by a lateral branching process.

ACTINOMYCES.

Meyen (Linnæa (1827) **2**, 433) described a fungus under the name *Actinomyces horkelii.* Bollinger (*Centrabl. f. d. med. Wiss.* (1877), **15**, 481) published an account of a disease in cattle caused by a vegetable organism which was carefully described and named *Actinomyces* by Harz (*Jahresb. d. k. Central-Thierarzneischule,*' München (1877–78), who at this time probably did not know of the previous occupation of the name by Meyen.

The work of Bollinger and Harz attracted much attention and was rapidly followed by a number of important contributions to the subject. For example, James Israel (*Virch. Arch.* (1878), **74**, 15; 50) described a similar organism as the cause of a similar disease in man and Ponfick (*Breslauer ärtzliche Zeitschrift*, May, 1879, and in subsequent publications) established the generic identity of the microörganisms in man and animals. The work of several writers showed that there existed varieties of this organism, but for a considerable time *Actinomyces* remained unquestioned as a generic name for the organisms.

Botanists classified the organisms in various ways, the most noteworthy being that of De Toni and Trevisan who created a new genus *Nocardia* (Saccardo, **8**, 927) and placed *Actinomyces* (Saccardo, **8**, 928) as a species with the following diagnosis:

"Glomerulis subglobulosis e filamentis densissime intertextis, fasciculos innumeros apice valde incrassato clavatos, a puncto centrali communi undique irradiantes constitutis."

OÖSPORA.

This generic name was introduced by Sauvageau and Radais (*Ann. Inst. Pasteur* (1892), **6**) to include the organisms previously described as *Actinomyces*, *Cladothrix*, and *Streptothrix*. This term never was seriously considered in the literature and needs no further notice.

NOCARDIA.

De Toni and Trevisan (Saccardo, **8**, 927) introduced *Nocardia* as the generic name and included as synonyms, *Streptothrix Actinomyces*, and in part *Discomyces*. The generic diagnosis given by them is as follows:

"Filamenta tenuissima, evaginata, articulata, Cladotricis more pseudoramosa, nunc e nucleo firmo radialiter expansa, nunc varie coalita. Arthrosporae in filamentis normalibus obvenientes, transformatione cocci singuli ortæ.—Est *Cladothrix* sine vaginis.

SPHÆROTILUS.

Engler (Syllabus der Pflanzenfamilien (1907), 5 ed., 5) places all the above-described organisms in the family *Chlamydobacteriaceae* of the *Schizomycetes*. He reduces the above-mentioned genera including *Actinomyces* to *Sphaerotilus* Kuetz (1833) the generic definition of which as given by De Toni and Trevisan (Saccardo, **8**, 926) is as follows:

"Filamenta premitus affixa, basi ab apice superiori distincta, initio simplicia, dein Cladotricis more pseudoramosa a basi ad apicem subæquilata, articulata, vagina gelatinosa obducta, in fasciculos crassos floccosos varie divisos consociata. Multiplicatio fragmentis filamentorum secedentibus, quae filamenta et fasciculos novos efficiunt. Arthrosporae numerosissimae, articulorum divisiones in tres directiones ortæ."

The above review shows the confusion which exists regarding the botany of the group of organisms which are variously recognized as *Streptothrix, Cladothrix, Actinomyces, Nocardia,* etc., and this seems to have been still further emphasized by workers in medicine and by other recent writers upon the subject. Some of the more important contributions are as follows:

Petruschky (Handbuch der Microörganismen, Kolle and Wassermann (1903), **2**, 832) classifies *Actinomyces*, *Streptothrix*, *Cladothrix* and *Leptothrix* as species of *Trichomyceta* of the *hyphomycetes*. He recognizes *Streptothrix* as the generic name of the parasites of mycetoma.

From the standpoint of an investigator in medicine, whatever may be the criticisms of botanists, the work of L. Gedoelst (Les Champignons parasites de l'homme et des animaux domestique, Paris, 1902) is particularly satisfactory, because of its simplicity of arrangement and attention to details. His classification places the organism under discussion among the *Fungi imperfecti* and in the genus *Discomyces* Rivolta (1878), with *Streptothrix* Cohn (1875); *Actinomyces* Harz (1877); *Nocardia* Trevisan (1889); *Oöspora* Sauvageau et Radais (1892) and *Discomyces* Blanchard (1900) as synonyms.

Foulerton (Allbutt's System of Medicine (1906), **2**, pt. 1, 302) who has been interested in this subject and has made many most important contributions to it, maintains *Streptothrix* Cohn to be the generic name. Foulerton gives four reasons for using *Streptothrix* in preference to any of the other terms.

1. He does not consider that Corda's indefinite use of the term in 1833 should make *Streptothrix* Cohn (1875) untenable.
2. This being acceptable, *Streptothrix* becomes the correct botanical name by priority of description.
3. *Streptothrix* was adopted by the committee of the Pathological Society.
4. It is by far the most generally used name.

James Homer Wright (Osler's Modern Medicine (1907), **1**, 327; 340) who has made valuable contributions to the study of *Actinomycosis* recognized *Nocardia* as the correct generic name, but raises Actinomyces from species, as given by Trevisan, to generic rank and thus converts what most authors have included in a single genus, into two genera.

Sir Patrick Manson (Tropical Diseases (1907), 4 ed., 759) in his recent discussion of mycetoma has adopted a liberal etiologic classification, both by his definition and his classification of the varieties of mycetoma. He classes actinomycosis as one variety of mycetoma, designating it as actinomycotic mycetoma, and the other names under discussion here might also be included in this category, if we adopt this definition. This eminent author in his definition of mycetoma terms it "a fungus disease of warm climates, affecting principally the foot, occasionally the hand, rarely the internal organs or other parts of the body."

Manson in this classification follows Brumpt (*Arch. Parasit.* (1906), **10**, 489) who in turn apparently adopts his classification of the parasites from Gedoelst (*loc. cit.*). The diverse forms of the disease recognized are:

I. Actinomycotic mycetoma caused by *Discomyces bovis* (Harz 1877). II. Vincent's white mycetoma produced by *Discomyces maduræ* (Vincent 1894). III. Nicolle's white mycetoma the result of *Aspergillus nidulans* (Eidam 1883). IV. Buffard's black mycetoma caused by *Aspergillus bouffardi* (Brumpt 1906). V. Classic black mycetoma from *Madurella mycetomi* (Laveran 1902). VI. Brumpt's white mycetoma from *Indiella mansoni* (Brumpt 1906). VII. Reynier's white mycetoma resulting from *Indiella reynieri* (Brumpt 1906). VIII. Bouffard's white mycetoma from *Indiella somaliensis* (Brumpt 1906).

SPECIES CONSIDERATION.

Following the generic name of the entire group of organisms under consideration, the next logical step of the problem is a discussion of the species properly belonging to the genus.

The classification of species is a more difficult problem than the generic determination, largely because of the imperfect description of many of the so-called species or varieties. In fact, but few have been described with sufficient clearness to make determination possible.

It is not possible to state who first recognized this group of organisms. It may have been Corda, 1842; Mayen, 1827; Von Langenbeck, 1845 (Acland in Allbutt's System (1906), **2**, pt. 1, 325); Sir T. Smith, 1855 (*ibid*); Lebert (1857) (Traité d'anatomie pathologique, **1**, 54); Ballingal, 1855; or any one of several other writers, some of whom undoubtedly saw these parasites in lesions of the human body.

However, Henry Vandyke Carter, working from 1859 to 1874, first established the pathogenic rôle of the streptothrices in human pathology. While Carter did not cultivate his organism on artificial media and his descriptions are insufficient for species determination, a study of his publications leaves no doubt but that he was working with a clinical type of *Streptothrix* infection and his observations as to the specific etiology were quite satisfactory.

Erye 1860, Collas 1861, Biddie 1862, Coquerel 1866 Moxon and Hogg (*Trans. Path. Soc.*, London (1870)), Bristowe (*Trans. Path. Soc.*, London (1871)), Hogg (*Med. Times & Gaz.*) (1871), all recognized fungus-like bodies in cases of foot infection, which were clinically mycetoma or Madura foot.

Berkeley (*Med. Press & Circ.*, (1876)) states that he had cultivated one of these organisms from a case of Madura foot which had been forwarded to him by Vandyke Carter. He named the organism *Chionyphe carteri*.

Rivolta (*Med. Vet.* (1868)) probably saw these organisms in pus taken from an abscess on the jaw of a cow. Rivolta (1868–1875) also found disc-like bodies in nodular masses from the tongue of a cow. He named the disease sarcomycosis.

Robin (Traité de Microscopie, Paris (1871), 575) gives a brief description of yellowish granules from two abscesses which were probably due to *Streptothrix* infection.

Heller (about 1872, completed a work which he published in *Deutsch. Arch f. klin. Med* (1885), **37**, 372) and from his description and drawing probably saw these organisms in the discharges from a case which he later considered to be acute actinomycosis.

Perroncito (1875) evidently saw and described species of this organism taken from a pseudosarcoma of the jaw of a cow.

Cohn (*Beitr. Biol. d. Pflanzen.* (1875)) **1**, 148, described an organism which he obtained from concretions in the lachrymal canals of a patient, terming it *Cladòthrix fosteri*.

Bollinger (*Deutsche Ztsch. f. Thiermed.*, Leipz. (1877), **3**, 334) noted the constant occurrence of a branching organism in lumpy-jaw of cattle; Harz (*ibid*, (1878)) described it, naming the organism *Actinomyces bovis* and Bollinger termed the disease actinomycosis.

Israel (*Virch. Arch* (1878), **74**, 15) described a disease in man similar to actinomycosis in cattle and detailed the microscopic appearances of the causative *Streptothrix*. Ponfick (*Breslau. ärztl. Ztschr.* (1879) furnished strong evidence of the etiologic identity of the diseases of man as described by Israel and of cattle as given by Bollinger and Harz.

Corre (*Arch. méd. Nav., Par.* (1883)) in reporting the notes of Dr. Collas called attention to the probable identity of actinomycosis with the earlier described mycetoma, and many other authors since that time have come to the conclusion that the diseases are probably the same.

Mandareau (*Bull. acad. méd.* (1887), **18**, 555) gave a morphologic description of a species of *Streptothrix*. Nocard (*Ann. Inst. Pasteur* (1888), **2**, 293) described and cultivated a *Streptothrix* from the lesions of a disease known as *farcin du boeuf* which was very prevalent among cattle in Guadeloupe. Organisms which agree with Nocard's description have repeatedly been isolated from pathologic lesions by other authors. Nocard's work was epoch making in that he was the first satisfactorily to cultivate a *Streptothrix* in pure culture.

Affanassiew and Schultz (*Münchener med. Wchnsoh.* (1889), **36**, 418) briefly described a *Streptothrix* obtained from pus and sputum. Cultures were pathogenic for guinea pigs. Protopopoff and Hammer (*Ztschr. f. Heilk.* (1890, **11**, 255) reported incomplete studies of the cultures of Affanassiew's and Schultz's organism. Kischensky (*Arch. f. exp. Path. u. Pharm.* (1889), **26**, 79) partially described and probably cultivated a *Streptothrix* which may have been identical with that cultivated later by Wolff and Israel from a human case of actinomycosis of the lungs. Bujwid (*Centrbl. f. Bakt., etc. Abth.* 1 (1889), **6**, 630) cultivated and briefly described a *Streptothrix* which was a facultative anaërobe taken from a human case of actinomycosis.

Eppinger (*Wien klin. Wchnsch.* (1890), **3**, 321) cultivated a *Streptothrix* from a brain abscess and a "pseudo tuberculosis of the lungs", the patient having manifested the clinical symptoms of meningitis during life. This organism was Gram positive, acid-fast and a facultative aërobe. Growth occurred on the ordinary laboratory media and the organism was pathogenic for laboratory animals. Eppinger's publication, like that of Nocard, forms a landmark in the history of the disease. His work has been confirmed by MacCallum and others and his organism, which is a different species from that of Nocard, will be more fully considered in this paper.

Almquist (*Ztschr. f. Hyg.* (1890), **8**, 189) cultivated species of *Streptothrix* from three different sources. The first was discovered as a contamination in a gelatin culture tube, the second was cultivated from pus taken from the base of the brain from a human case and the third culture was isolated from water. Liebman (*Arch. per le sci. med.* (1890), **14**, 361) discussed the cultivation of *Streptothrix* in pure culture.

Bostroem (*Beitr. z. path. Anat., etc.* (1891), **9**, 1 to 240) cultivated a single species of *Streptothrix* from eleven cases of actinomycosis. His organism was Gram positive and in part acid-fast and was a facultative aërobe in cultures. Growth was obtained with difficulty directly from the lesions, but the later transplants were more satisfactory in artificial media. Bostroem's article was the first published exhaustive consideration of the cultivation of *Streptothrix*. Wolff and Israel 1891 (*Virch Arch.* (1891), **126**, 11) cultivated a *Streptothrix* from two cases of clinical actinomycosis in man. In one case the lesion was a retromaxillary tumor and the other was actinomycosis of the lungs. This organism was acid-fast and a facultative anaërobe. Gruber (*Tr. VII Intern. Cong. Hyg. & Demog.*, Lond. (1891), **2**, 65) discovered (as an accidental contamination of culture media) an organism which he described as *Micromyces hofmanni*. This organism produced pyæmia in animals and "ray fungus" types were present in the lesions. The articles by Doyen (*Tr. VII Intern. Cong. Hyg. & Demog.*, Lond. (1891), **3**) and Roussel (These, Paris, 1891) are not available to us.

Hesse (*Deutsche Ztschr. f. Chir.* (1892), **34**, 274) obtained a *Streptothrix* by culture from an abscess in the groin, which when opened was found to communicate by a sinus with the intestine. Autopsy on the patient, who died after more than a year's illness, showed a rectal fistula communicating with multiple abscesses in and around the pelvis. There was bronchitis, but the organisms were not found in the sputum. The organism was Gram positive and aërobic in culture media. Growth occurred on the majority of media and serum media were liquefied. No positive results were obtained from intravenous, intraperitoneal, or subcutaneous injections of cultures into rabbits, guinea pigs or white mice. Sauvageau and Radais (*Ann. Inst. Pasteur* (1892), **6**, 242) studied a number of streptothrices which had already been isolated by other authors. They made a classification of *Streptothricae* in general, based upon cultural characteristics.

The articles by Lanz (*Cor. Bl. f. schweiz. Aerzte* (1892), 307; 339); Ebermann (Inaug. Diss. St. Petersburg (1893); Dor (*Gaz. hebd. de med.* (1893) 2 s., **30**, 40) and of Dor and Bérard (*Prov. méd.* (1893) are not available to us.

Vincent (*Ann. Inst. Pasteur* (1894), **8**, 129) cultivated a *Streptothrix* which was pathogenic for laboratory animals from a case of ochroid variety of mycetoma. We have already noticed this organism somewhat in detail and it will be considered further. Vincent's work is very important because he was the first satisfactorily to cultivate a *Streptothrix* from the Madura foot type of the disease and because his organism is specifically different from any of those described before his paper appeared. Boyce and Surveyor (see bibliography) in a series of articles, described streptothrices which they were able to isolate from cultures made by friends in India, taken from cases of mycetoma and forwarded to the authors in England. The brief description given by these authors renders it probable that this organism was identical with that of Vincent. Karg (Ref. Düms' *Deutsche mil-ärztl. Ztschr.* (1894), **23**, 145) cultivated a *Streptothrix* from a case of actinomycosis in man. Karg considered his organism to be identical with that of Bostroem. This author also reported a second case of the disease with results similar to those obtained with the first one. Leith (*Edinb. Hosp. Rep.* (1894), **2**, 121) and Newjadomsky (Ref. Lubarsch and Ostertag Ergb. (1898), **5**, 665) each isolated by culture a *Streptothrix* from a human case of actinomycosis. The article of Kitchensky (*Arch. f. exper. Path. u. Pharmakol.* (1890), **26**, 79) is not available to us. Sabrazès and Rivière (*Presse méd.* (1894), Sept. 22) reported the cultivation of a *Streptothrix* from abscesses in the brain, lungs, and kidneys of a human case. This organism only grew anaërobically. In their second case (*Mercredi méd.* (1895), 485) an aërobic *Streptothrix* was cultivated from the sputum and subcutaneous abscesses of a patient. Both these organisms are reported as being pathogenic for small animals, the latter one, however, only producing lesions when injected together with dilute acetic acid.

Aschoff (*Ber. klin. Wchnsch.* (1895), **32**, 738) cultivated a *Streptothrix* from a case of human actinomycosis and stated that he had produced actinomycotic lesions in animals by inoculating cultures of the organism.

Du Bois Saint-Sevrin (*Semaine méd.* (1895)) cultivated a *Streptothrix* from a case of ulcer of the cornea in a human patient with a pseudomembranous conjunctivitis. Ferré and Faguet (*Mercredi méd.* (1895), 441) did the same from an abscess in the *centrum ovale* of the brain. The authors considered this organism to be identical with that of Eppinger. Rullmann (Ref. *Centralbl. f. Bakt., etc.* (1895), **17**, 884) cultivated a *Streptothrix* from soil and again in 1898 the same author (*Münchener med. Wchnsch.* (1898), **45**, 919) cultivated what he apparently considered to be the same organism from a case of disease of the lung. It was a *Streptothrix* positive to Gram's stain, which grew on ordinary media as a facultative aërobe. Positive local lesions were produced in rabbits, guinea pigs, and mice when these animals were inoculated with cultures. Garten (*Deutsche Ztschr. f. Chir.* (1895), **41**, 257) cultivated a *Streptothrix* from lesions in a human case. There was necrosis of the vertebrae and ribs, with abscesses, sinus formation and empyæma. This organism grew on laboratory media and was pathogenic for three out of thirty-seven rabbits and guinea pigs.

Dor (*Gaz. hebd. d. méd.* (1896), **43**, 553) obtained a *Streptothrix* from an actinomycosis-like abscess at the angle of the jaw. The pus contained granules with long, beaded filaments which did not stain by Gram's method. The organism grew aërobically on liquid media only. Sawtschenko (*Baumgarten's Jahresb.* (1896), **12**, 613) cultivated an organism from a case which he termed pseudoactinomycosis. It formed long threads which did not stain by Gram's method and which grew only under anaërobic conditions. Jurinka (*Mitth. a. d. Grenzgeb. d. Med. u. Chir.* (1896), **1**, 139) cultivated a *Streptothrix* from a human case of actinomycosis which he considered identical with that of Wolff and Israel. The article by Kozerski (Ref. *Jahresb. d. ges. Med.* (1896), **2**, 223) is not available to us.

Scheele and Petruschky (*Verhandl. d. Con. f. innere Med.* (1897), **15**, 550) cultivated a *Streptothrix* which was acid-fast by the Ziehl-Neelsen method from the sputum and subcutaneous abscesses of a case of pyæmia, pleuro-pneumonia, cystitis, and pyelitis. It grew on agar, gelatin, and broth. Its pathogenic character for animals apparently was not determined. Buchholtz (*Ztschr. f. Hyg.* (1897), **24**, 470) described a *Streptothrix* found in the lung of a patient suffering from a disease which, both clinically and pathologically, very closely resembled tuberculosis of the lungs. The organism was Gram positive and acid-fast, but did not grow on artificial media. Urban (*Münchener med.*

Wchnsch. (1897), **44**, 124) cultivated a *Streptothrix* from a case of human actinomycosis. Berestnew (Aktinomykose und ihre Erreger (Dissert), Moskau (1897) reported several cases. A *Streptothrix* was cultivated from a subperiostial abscess of the lower jaw of a woman (Case I). This clinically was a case of "lumpy jaw." This organism was a *Streptothrix*, facultative anaërobic, Gram positive, dying after three generations on artificial media. It was not pathogenic for rabbits, guinea pigs, or tame mice. The organism from his Case II was cultivated from an abscess under the right nipple of a 16-year-old patient who had symptoms of disease of both lungs. The organism differed from that of Case I in that it grew somewhat better in the presence of oxygen. The cultures in Case III were from sputum and chest sinuses in a patient forty-four years of age, who died after an illness of about one year. The organism was Gram positive, facultative aërobic, and grew best in bouillon. It was neither fatal for rabbits nor guinea pigs when injected either intraperitoneally or subcutaneously; a temporary infiltration of the tissues resulted by the latter method. Abel (*Münchener med. Wchnsch.* (1897), **44**, 124; 149) made brief reports of a pathogenic *Streptothrix* from sputum. Van Neissen (*Virch. Arch.* (1897), **150**, 482) worked with an organism which was not differentiated from that of Wolff and Israel.

Berestnew in another case (*Ztschr. f. Hyg. u. Infectionskrankh.* (1898), **29**, 94) obtained a *Streptothrix* in pure culture from the lesions in a child suffering from an abscess of the lung and pyæmia. This organism was negative to Gram, grew anaërobically on media and was pathogenic for animals. Petruschky (*Deutsche med. Wchnsch.* (1898), **24**, Ver.-Beil. 78) cultivated an organism similar to that of Scheele and Petruschky (*loc. cit.*) from the sputum obtained from a second case of streptothricosis. Alissow and Skworzow (ref. Lubarsch and Ostertag (1898), **5**, 664) studied two cases of streptothricosis in man. They obtained two organisms in bouillon cultures, a bacillus and a *Streptothrix* growing in symbiosis. Pure cultures of the *Streptothrix* developed only clubs and rods, but when bacteria were again mixed in the cultures, long fungus threads were produced. The authors consider the lesions to be due to the mixed infection. Schtscheglow (1898) (*ibid.*), also secured mixed cultures and the bacteria present influenced the morphology of the *Actinomyces*. Newjadomsky (1898) (*ibid*) reported one case in man in which a *Streptothrix* was obtained in pure culture from a subdiaphragmatic abscess. The author considered the organism to belong to a new species. It was not pathogenic for guinea pigs. Rullman (*Münchener med. Wchnsch.* (1898), **45**, 919) cultivated a *Steptothrix* from the sputum of a patient with a localized lesion near the root of the right lung. This organism was Gram positive and grew on all media. It was pathogenic for mice, rabbits and guinea pigs, and could be reclaimed by culture from lesions in these animals. Grillo (*Reforma Medica* (1898), **14**, 301) cultivated a *Streptothrix* from a case of human actinomycosis and from the bovine infection and reproduced the disease by animal inoculation with cultures of the organism. Harbitz (*Norsk Mag. f. Lægevidensk* (1898), **13**, 1) obtained a *Streptothrix* by culture from five cases of human actinomycosis. Flexner (*Journ. Exp. Med.* (1898), **3**, 435) reports a case of human infection with a *Streptothrix*, but his organism did not grow on artificial media. The article by Marwedel (*Beit. z. klin. Chir.* (1898), **21**, 561) is not available to us.

Foulerton (*Lancet* (1899), **2**, 779) cultivated his *Streptothrix hominis* from abscesses of the chest with deep sinuses in a patient showing symptoms of a severe lung involvent with pyæmic symptoms. This author (see bibliography) has also made numerous other contributions to the morphology of the subject and has probably done more than any other toward clearing up the confusion which exists regarding this group of organisms. Levy (*Centralbl. f. Bakt., etc.* (1899), **26**, 1) cultivated a *Streptothrix* from five cases of clinical actinomycosis in man. He considers his organism to be identical with that of Wolf and Israel. Paul Krause (*Centralbl. f. Bakt., etc.* (1899), **26**, 209) obtained a *Streptothrix* from an abscess of the lower jaw. It was Gram positive but not acid-fast, a facultative aërobe and grew on ordinary laboratory media. No positive results were obtained by intraperitoneal or subcutaneous injection of cultures into rabbits, guinea pigs, or white mice. Hayo Bruns (*Centralbl. f. Bakt., etc.* (1899), **26**, 11) cultivated a *Streptothrix* from a lesion which according to the diagnosis was an actinomycotic abscess of the abdominal wall. The organism was Gram positive, but not acid-fast and did not stain well with the ordinary aniline dyes. Growth occurred on ordinary media, best under aërobic conditions. No lesions were produced by intravenous, intraperitoneal, nor subcutaneous injections of cultures in rabbits, guinea pigs, or mice. Silberschmidt (*Ann. Inst. Pasteur* (1899), **13**, 841) obtained a *Streptothrix* by culture from the lungs of a goat which had a disease closely resembling tuberculosis. This organism was carefully described by the author and later by Foulerton and Jones, (*Tr. Path. Soc.* (1902), **53**, 99) who considered it to be a new species and our work is in accord with this conclusion.

Brault (*Arch. d. parasit.* (1899), **2**, 535) observed two human cases of actinomycosis. He cultivated a *Streptothrix*, at first in symbiosis with bacteria and later in pure cultures. His organism grew on ordinary media and was pathogenic for animals.

Norris and Larkin (*Journ. Exp. Med.* (1900), **5**, 155) obtained a *Streptothrix* by culture from two cases of bronchopneumonia and bronchiectasis. Both cases proved fatal. This organism was Gram positive, but not acid-fast by the Ziehl-Neelsen method. The authors consider it probably to be identical with Israel's *Streptothrix*. Local lesions were produced in both rabbits and guinea pigs by injection of the cultures. Cozzolino (*Ztschr. f. Hyg. u. Infectionskranfh.* (1900), **33**, 36) reports a human case of *Streptothrix* infection of the ear. He cultivated an organism from the lesion which was pathogenic for mice and guinea pigs and described it very well. It was a facultative aërobe, but branching was not observed.

Dean (*Tr. Path. Soc.* (1900), **51**, 25) cultivated a *Streptothrix* from the lesions in a horse which clinically was suffering from actinomycosis. He considered his organism to be a new species, differing in certain particulars from any described previously. This organism was a facultative aërobe, Gram positive, and grew very poorly on the majority of media and not at all on others. It was pathogenic for animals, producing lesions which contained organisms resembling *Actinomyces*, with club-shaped ends. However, in cultures no club formations were observed. Tusini (*Arch. f. klin. Chir.* (1900), **62**, 249) observed four cases of *Streptothrix* infection in man. The one reported in detail was an infection which clinically was Madura foot. From this case, he cultivated a *Streptothrix* which was pathogenic for guinea pigs and which in cultural characteristics closely resembled the organism of Vincent. Sternburg (*Wien. klin Wchnsch.* (1900), **13**, 548) cultivated a *Streptothrix* resembling that of Wolff and Israel from three cases of human actinomycosis.

Aoyoma and Miyamoto (*Mitth. a. d. med. Fac. d. k. jap. Univ. a. Tokio* (1901), **4**, 231 to 276) obtained a *Streptothrix* in pure culture from an abscess of the lung. This was Gram positive, acid-fast, and a facultative aërobe; pathogenic for rabbits, white mice, and hens. The authors believed their organism to be very closely related to or identical with *S. eppingeri*. Mertens (*Centralbl. f. Bakt., etc.* (1901), **29**, 649) reported one human case and cultivated a *Streptothrix* from the lesions. Cultures at first only grew in bouillon, but gradually growth on other media was successful. The anaërobic tendencies of his organism were changed so that it grew aërobically after a considerable time on artificial media. This organism produced lesions in the eyes of rabbits. Silberschmidt (*Ztschr. f. Hyg. u. Infectionskrankh.* (1901), **37**, 345) studied eight cases of *Streptothrix* infections in man. He cultivated the organism and believed he had isolated three different species. In six of his eight cases the organisms closely resembled those of Wolff and Israel. The others more closely approximate Bostroem's organism. Jelenewski (Ref. *Baumgarten's Jahresb.* (1901), **17**, 495) studied fifty cases of actinomycosis occurring in the mouths of animals. He cultivated the fungus first with *B. subtilis*. Later he obtained pure cultures both aërobically and anaërobically. Cultures of the organisms were pathogenic for calves, but not for rabbits and guinea pigs. The author concluded that his *Streptothrix* was a new species, basing his decision upon both its cultural and pathogenic properties.

Foulerton and Jones (*Tr. Path. Soc.* (1902), **53**, 56) studied the group extensively and described some new species. The tentative classification by these authors was the most satisfactory which had been made up to the time of its publication.

They also cultivated a *Streptothrix* ((ibid), **75**, 93) which they believed to be the cause of the disease, from a conjunctivitis and keratitis in a twelve year old girl. The organism was Gram positive, but not acid-fast; a facultative aërobe growing on all media. It was not pathogenic for rabbits, guinea pigs, or white mice. The same authors (*ibid*, 100) isolated a *Streptothrix* from "a case of pulmonary infection in a woman." This organism was Gram positive, not acid-fast, grew on the usual laboratory media, and was not pathogenic for rabbits. MacCallum (*Centralbl. f. Bakt., etc. orig.* (1902), **31**, 529) cultivated a *Streptothrix* which he considered to be identical with that of Eppinger from the peritoneal exudate in the body of a child dead of subacute purulent peritonitis which followed a surgical operation for relief of stricture of the oesophagus. Birt and Leishman (*Journ. Hyg.* (1902), **2**, 120) studied a *Streptothrix* which was obtained from a fatal human case. Empyæma, pericarditis, and "cirrhotic nodules in the lungs" were present at autopsy. The organism was isolated from the pleuræ, pericardium, and lung. It was Gram positive and acid-fast and showed strong aërobic tendencies. It grew on the majority of media, producing a coral-pink color. This organism was pathogenic for guinea pigs and is probably identical with Eppinger's *Streptothrix*. Schukewitsch (Ref. *Jahresb. d. ges. Med.* (1902), **1**, 711) cultivated a *Streptothrix* somewhat resembling that of Wolff and Israel from twenty-two out of twenty-five cases of human actinomycosis. Von Baracz (*Arch. f. klin. Chir.* (1902), **68**, 1050) reports on fifty-two cases of actinomycosis. The article is a splendid monograph, but does not go extensively into the question of the etiology of the disease. Welleminsky (*Deutsche med. Wchnsch.* (1902), **28**, Ver.-Beil. 196) cultivated a *Streptothrix*-like organism, nonpathogenic for animals, from lesions in one case.

Trolldenier (*Ztschr. f. Thiermed.* (1903), n. s. **7**, 81) reports a case of actinomycosis in a dog. He cultivated a *Streptothrix* which he considered to be a new species from the lesions. The organism was pathogenic for mice and guinea pigs, rabbits, dogs, and calves. Doepke (*Münchener med. Wchnsch.* (1903), **50**, II, 2245) studied several human cases and cultivated organisms which where similar to that of Wolff and Israel. Lignières and Spitz (*Arch. d. parasitol.* (1903), **7**, 428; *Centralbl. f. Bakt., etc.* (1904), **35**, 294; 452) cultivated a *Streptothrix* from a calf suffering from actinomycosis which they considered similar to that of Wolff and Israel. The article by Horst (*Ztschr. f. Heilk., Abt. f. path. anat.* (1903), **24**, 157) is not available to us.

James Homer Wright (*Journ. Med. Research* (1904), **13**, 349) cultivated what he believes to be a single species of *Actinomyces* from 13 cases of human actinomycosis and two cases of the bovine disease. He considers his organism to be of the same species, if not identical, with that of Wolff and Israel. This article is the most thorough study of one species of this group of organisms that has yet been made. Stokes (*Am. Journ. Med. Sci.* (1904), n. s. **128**, 861) obtained a *Streptothrix* from an abscess of the lung. This organism was acid-fast, grew aërobically and was pathogenic for laboratory animals. Schabad (*Ztschr. f. Hyg.* (1904), **47**, 41) considers the true *Actinomyces* and the organisms of Bostroem or Eppinger to be different species. He cultivated from the sputum and abscess of the breast in one human case an organism which he considered to be identical with that of Eppinger in its morphology, biology, and pathogenicity. Hartman (*Tr. Chicago Path. Soc.* (1904), **6**, 157) cultivated a *Streptothrix* from one human case. The articles by Tuttle (*Med. and Surg. Rep. Presbyterian Hosp.* N. Y. (1904), **6**, 147) and McDonald (*Scot. Med. & Surg. Journ.* (1904), **14**, 305) are not available to us.

Pinoy (*Comp. rend. acad. sci.* (1906), **143**, 1175) isolated a *Streptothrix* and claimed to have experimentally reproduced the black granules by inoculation of cultures into a pigeon's foot. His organism was a facultative anaërobe. Nicolle and Pinoy (*Arch. d. parasitol.* (1906), **10**, 437) cultivated a *Streptothrix* from a case of mycetoma in an Arab.

Musgrave and Clegg (*This Jurnal, Sec. B.* (1907), **2**, 477) obtained a culture from the sinuses in a case of the ochroid variety of mycetoma occurring in a Filipino woman in Manila. The cultural characteristics have already been described and will be further discussed. Poppenheimer and Satchwell (*Journ. Infect. Dis.* (1907), **4**, 617) report a case of endocarditis and isolation of a pleomorphic bacterium resembling somewhat closely the *Streptothricæ*. They review the literature of *Streptothrix* infections in man and tentatively classify their organism as a *Cladothrix*. The report of these authors is thorough and complete and from their description it does not seem as if their organism could properly be considered under *Streptothricæ*.

Strong cultivated a *Streptothrix* from a case of mycetoma in India. This organism is undoubtedly identical with that of Vincent.

OTHER STREPTOTHRICÆ.

In addition to the pathogenic organisms of the group under discussion and which have been isolated from pathologic lesions in man and animals, others have been cultivated from sputum, pus, or other human excreta under circumstances which make their exact source questionable; there are still others which have only been described as being obtained from animals; and some have been cultivated only from air, water, soil, and other outside sources. The following may be mentioned: *S. rubra* of Ruiz-Casabó (ref. *Centralbl. f. Bakt., etc.* (1895), **17**, 466) isolated from sputum; *Cladothrix mordoré* of Thiry (*Arch. d. physiol.* (1897), **29**, 284) obtained from an anginal exudate; the *Streptothrix* of Dean (*Tr. Path. Soc.* (1900), **51**, 26) isolated from an abscess of the jaw in a horse; and *S. lacertæ* of Terni (ref. *Centralbl. f. Bakt. etc.* (1896), **19**, 953) isolated from nodules in the liver of a lizard. Rossi-Doria (*Ann. d. l'Ist. d'ig. sper. d. Univ. di Roma* (1891), **1**) cultivated a *Streptothrix* from a case of bovine actinomycosis. Sanfelice (*Centralbl. f. Bakt. etc., orig.* (1904), **36**, 355; and *Arch. f. wiss. u. prakt. Thierheil.* (1896), **22**, 153) obtained *Streptothricæ* from several minor cases of bovine actinomycosis. He considered his organisms to be similar to those of Gasperini and Doria. Gasperini (*Proc.-verb. Soc. Tosc. di Sci. Nat.* (1895), **9**, 64; 292) isolated and described two strains of *Streptothrix* from actinomycosis in cattle. He (*Ann. d. l'Ist. d'ig. sper. d. Univ. di Roma* (1892), **2**, 167; *Proc.-verb. Soc.*

Tosc. de. Sci. Nat., July 5, (1896) also worked with a number of cultures obtained from other authors including that of Dessy (*loc. cit.*). With this latter organism. he stated that he had produced typical actinomycosis by injection into the jaw of a cow.

Lange and Manasse (ref. Levy. *Centralbl. f. Bakt. etc.* (1899), **25, 5**) isolated a *Streptothrix* somewhat resembling that of Wolff and Israel from actinomycosis in a dog. Bahr (*Ztschr. f. Thiermed.* (1904), n. s. **8**, 47) cultivated a *Streptothrix* from an actinomycosis-like disease in a dog. Dean (*Tr. Jenner Inst. Prevent. Med.* (1899), **2**, 17) did the same with an organism resembling that of Wolff and Israel, obtained from an abscess in the jaw of a horse and this *Streptothrix* was pathogenic for animals. Mosselmann and Liénaux (*Ann. d. méd. vet.* (1890), **39**, 409) obtained a *Streptothrix* from a case of bovine actinomycosis.

Lignières and Spitz (*Bull. Soc. centr. d. méd. vet.*, Paris (1902), **56**, 487) cultivated a bacillus from cases of clinical actinomycosis in cattle. They state they produced true actinomycosis, the organism showing the club-shaped *Streptothrix* granules, with cultures of this organism, by inoculation of their cultures into cattle.

The *Streptothrix* of Caminiti (*Centralbl. f. Bakt. etc., orig.* (1907), **44**, 193) is one of the most important of the organisms cultivated from the air, because of its pathogenic properties and close cultural resemblances to the *Streptothricæ* which produce clinical actinomycosis. This organism is Gram positive, acid-fast in part, a facultative aërobe with anaërobic preferences, liquefies gelatin and produces pigment in varying amount and color in artificial media. It is pathogenic for all animals experimented upon, producing circumscribed local lesions by injection of cultures.

Other organisms of this class which may be mentioned are *S. leucea* Foulerton (*Tr. Path. Soc.* (1902), **53**, 101) isolated from sewage and water; *S. alpha* Jones (*ibid*, 102); *S. erythrea* Foulerton (*Ibid*, 107) from culture tubes prepared with horse serum; *S. beta* Jones (*ibid*, 109); *Cladothrix invulnerabilis* of Acosta and Grande Rossi (ref. *Centralbl. f. Bakt, etc.* (1893), **14**, 14); the *Streptothrix* of Kedzior (*Arch. f. Hyg.* (1896), **27**, 328) isolated from sewage and water; *S. albido-flava, S. carnea*, and *S. aurantiaca* of Rossi-Doria (*Ann. d'Ist. d'ig. d. Roma* (1891), **1**) isolated from air; *Micromyces hoffmanni* described by Gruber (ref. *Centralbl. f. Bakt., etc.* (1891), **10**, 648) isolated from air.

Several other brief descriptions of *Streptothricæ* from pathologic lesions might be noticed, but the principal ones have been mentioned above. The technical descriptions have for the greater part been omitted in this review of the literature, but it may be stated that a classification of this material which will be satisfactory to all is scarcely possible. However, several authors have attemped an arrangement of species and varieties.

Foulerton worked with a large collection of cultures obtained from various sources. He redescribed and renamed several species, both pathogenic and non-pathogenic, the classification being based largely upon morphologic and cultural characteristics. Rossi-Doria occupied himself for the greater part with *Streptothricæ* cultivated from extraneous sources and his classification is based upon the character of the cultures obtained. Gaspereni gave a classification based upon cultural characteristics. Brumpt (*Arch. d. parasitol.* (1906), **10**, 489) recognized several species and more than one genus. Wright worked with one species and gave the most complete description of that organism to be found in literature. His "*Hyphomycete*" cultivated from a case of the "black variety" of mycetoma evidently was not a *Streptothrix* and therefore is not included in the discussion in this paper. Caminiti recognizes forty-one species based upon his own work and a review of the literature. Manson's classification refers particularly to mycetoma and has already been noticed.

If we carefully study the literature of species determination, it will be found in greater part to be only of historic interest and value. The work is generally too incomplete to be final for species determinations, and in cases even the generic position of the described parasites is doubtful. For this reason we have considered only the technical descriptions of the organisms which have been cultivated and described with sufficient accuracy and completeness to make them available for comparative purposes. Much of the work of the older writers was well done when due consideration is given to the technique developed at the time of publication, and this work should always be kept before us in giving historical summaries. However, for purposes of further study and for comparison, having in view the harmonizing of our ideas regarding these infections, it seems to us that the following are the principal publications regarding *Streptothricæ,* which have been isolated from pathologic lesions of man or animals.

1. Nocard (1888); 2. Eppinger (1890); 3. Almquist (1890); 4. Bostroem (1891); 5. Wolff and Israel (1891); 6. Hesse (1892); 7. Vincent (1894); 8. Boyce and Surveyor (1894); 9. Aschoff (1895); 10. Du Bois Saint-Sevrin (1895); 11. Sabrazès and Rivière (1894) (A and B); 12. Rullmann (1895); 13. Dor (1896); 14. Sawtschenko (1896); 15. Scheele and Petruschky (1897); 16. Bucholtz (1897); 17. Berestnew (1897); 18. Rullmann (1898); 19. Silberschmidt (1899); 20. Brault (1899); 21. Cozzolino (1900); 22. Dean (1900); 23. Aoyoma and Miyamoto (1901); 24. Jelenewski (1901); 25. Foulerton (1902) (3 or more species); 26. Trolldenier (1903); 27. Pinoy (1906). The work of Musgrave and Clegg (1907) might also be included in this list.

The twenty-eight species or varieties to be taken from this list are considered with due regard to the manner in which they are described by the authors. It is certain that they do not all represent different species and it is probable that some of the other organisms not included do belong to new species. Many of the articles in the literature are incomplete, and a careful study of such descriptions as are given convinces us that not more than ten different species are represented in the group. Several of the varieties may show slight morphologic and biologic differences, but these are not sufficient to warrant their being classed as separate species.

GENERAL DISCUSSION AND CONCLUSIONS.

The subject of streptothricosis or nocardiosis becomes somewhat simplified if the results of our own work are combined with those taken from the literature, but we realize fully that after considering all possible evidence, points must still remain open for discussion, and complete harmony regarding this subject can only be obtained by common adoption of a somewhat arbitrary classification.

DETERMINATION OF GENUS.

It is difficult to determine upon the correct name of the diseases, because of the botanical confusion regarding the position and designation of the group of organisms concerned, and of the lack of clearness of definition specifying definite limitations for the organisms to be included as the etiologic factor.

Both *Streptothrix* and *Actinomyces* are untenable as generic names if we strictly follow the rules of nomenclature, because they are not entitled to priority in the literature which belongs to *Nocardia;* besides both *Streptothrix* and *Actinomyces* are open to the objection that they have not received a sufficiently clear botanical definition and both names have been used in too uncertain a sense in the past. *Actinomyces* has also, unfortunately, been taken into recent literature with practically two definitions. The objections to *Nocardia* are as follows: (1) The published definition erroneously states that the branching is "false branching;" (2) the name has not been sufficiently accepted by botanists to insure permanency and (3) usage is very much against it, particularly as in some of the recent writings its meaning has been limited to include only a portion of the organisms which surely belong in the genus. Considering the confusion in botanical literature and the uncertainty, and therefore the liability to change which pertains to this nomenclature, we have, as stated in the introduction, chiefly because of usage, and therefore somewhat arbitrarily, tentatively accepted *Streptothrix* as the generic name of the organisms concerned, and streptothricosis as the designation of the disease caused by this group of branching, filamentous organisms. In making this decision we are fully aware of the rights of those who favor *Actinomyces* or *Nocardia,* and under the circumstances are tempted to introduce a new name (*Carterii*) for the genus, together with a full and complete definition.

Whatever the nomenclature, it is a fact that we have here a group of closely allied vegetable parasites of man and animals, which have the following principal characteristics:

Branching, filamentous organisms which develop into colonies made up of the organisms and "transformation products." The terminal hyphæ may or may not be radially placed on the surface of the colony and they may or may not develop "clubs." The group in general take Gram's stain and several members show acid-fast properties in a varying degree.

The organisms grow on artifical media, differing in their requirements for oxygen and in pigment production. To a less degree they show other variations in appearance on artificial media.

The majority of the organisms produce lesions in monkeys, which histologically resemble those found in the human infections and in those of other animal diseases caused by members of this genus.

This group or genus is closely allied to other genera of somewhat similar characters, the latter ranging from the branching bacteria through the nonbranching filamentous *Leptothrix* and the pseudo-branching *Cladothrix,* to the budding *Oïdia* or *Blastomyces.*

The only question of doubt regarding the expediency of our generic classification is raised by the very thorough and exhaustive work of James Homer Wright, who has brought forward some strong arguments in favor of making two genera out of the group of organisms under discussion.

As may be remembered, Wright separates this group into two genera; *Actinomyces* and *Nocardia.* He defines *Actinomyces* accurately and places all the organisms which he thinks do not come within this definition into the genus *Nocardia.*

Actinomycosis is defined as:

> "A suppurative process combined with granulation tissue formation, the pus of which contains characteristic granules of 'drusen' composed of dense aggregates of branched filamentous microörganisms and their transformation of degeneration products. In the term transformation products are included the characteristic, refrangent, club-shaped bodies radially disposed at the periphery of the granule, for these bodies have long since been clearly shown to arise by a transformation of the peripheral filaments. They may or may not be present at the periphery of the granule."

Wright, in his further discussion of the organisms, emphasizes the following points as being characteristic of *Actinomyces.*

Club formation in tissues, anaërobism, granule formation, peculiarities in culture media, morphology and action when injected into laboratory animals. However, some of these distinctions were not constant even in the author's series of cases.

If we accept Wright's definition of actinomycosis, some of the organisms termed *Nocardia* by the author must be included as etiologic factors in actinomycosis, because the requirements are fulfilled by microörganisms not included in his description of the organism which he considers the specific cause of the disease, and furthermore, if his definition and description of *Actinomyces* be accepted as sufficient for genus determination, other genera could be removed from the group with almost, if not with equally good cause. However, some of the principal characteristics given for *Actinomyces* are not peculiar to his organisms. Most of these are differences in *degree only* from other members of the group, and are not specific, and in some instances, as we have demonstrated by work with original cultures, Wright's conclusions, based upon a study of the literature, are wrong. His observations regarding *S. capræ* Silberschmidt, and *S. maduræ* Vincent are examples of this. Wright states that Vincent's case was probably one of actinomycosis, and that Silberschmidt worked with mixed cultures. We have had cultures from the original strains of both these organisms in our hands and are able to state positively that the bacillus- and coccus-like forms of *S. capræ* described by Silberschmidt are forms of the pure culture and not bacterial contamination. As to Vincent's case, the organism is distinctive and can not possibly be included in Wright's definition of *Actinomyces;* indeed, it forms one end of the *Streptothrix* group, while the *Actinomyces* of Wright forms the other.

SPECIES DETERMINATION.

Species determination in this genus is made extremely difficult, and classification of all the forms which have been given in the literature is impossible, because of the incomplete and imperfect descriptions which are given. Several of these descriptions are old, have not been repeated or confirmed, and are lacking in the elucidation of important points which are now recognized as essential for diagnosis. Our correspondence has elicited the fact that cultures of several of these species are no longer obtainable, and therefore, no further study of them can be made. Fortunately, we have been able to secure cultures of the most important members of the group and by comparative morphologic and biologic studies, particularly with reference to their pathogenic character, we have been able somewhat to simplify the classification by showing that some of the described species are identical. This includes *S. freeri,* which from a study of the literature we thought to be a new species, but after comparative study found to be identical with *S. eppingeri* in all essential particulars.

Another difficulty in establishing species or varieties is encountered in attempting to fix the amount of variation necessary to constitute a new species. The differences between various members of the group are practically in every instances those of degree only. For example; in the requirements for oxygen we have variations from facultative anaërobism with strong tendencies toward being negative to oxygen, as exemplified by the Wolf, Israel and Wright type of *Actinomyces,* to facultative aërobism with strong oxygen requirements, as exemplified in *S. eppingeri;* while other strains show intermediate stages of aërobiosis. Although strict anaërobes and equally strict aërobes have been mentioned, the conclusions probably are based upon errors in technique. Certainly this is true with the organisms with which we have worked, for in no instance have we encountered either a strict anaërobic, or an equally strict aërobic *Streptothrix,* although some of the cultures under our hands have had such properties ascribed to them by others.

Staining reactions.—The terminal filaments in lesions and young cultures usually stain very well by the usual aniline dyes, but in older colonies the central detritus does not stain and the filaments give irregular staining reactions often showing irregular, including coccus- and bacillus-like, forms. The reaction to Gram's solution is somewhat variable, depending upon the age of the colonies and there is some variation between the different species or varieties. However, in general, all strains are Gram positive to a greater or less degree.

Differences in *acid fast* properties have been used as being diagnostic in a number of described species, while unfortunately in others they have not been mentioned. These are important points in differentiation, but unfortunately such properties are a somewhat variable manifestation, depending in part upon the age and environment of the parasite and perhaps also upon other conditions, the nature of which is not clear. As with the oxygen requirements, degrees from the marked acid fast properties of *S. eppingeri* through those organisms showing the tendency only in certain portions, to *S. maduræ* which has no such properties are noted. *S. eppingeri,* often when taken from animal lesions and sometimes for example in cultures, will show acid fast properties which involve the entire organism, while in other cultures only portions of the organism will retain the fuchsin when decolorized and counter stained with Gabbet's stain.

Pigment production under certain circumstances is a property of most of the organisms of this group, as the cause of this is unknown and the result is variable, its diagnostic importance is lessened. Under like conditions, the color and general appearance of the pigment in any of these strains is usually fairly constant, but sometimes, particularly in animal tissues, it may show a more intense color. For example, *S. maduræ,* which usually produces a reddish-pink pigment in cultures, may, when inoculated into monkeys, at one time give a similarly colored pigment or again one considerable darker; so dark in fact as to appear almost black to the naked eye. The pigment of *Actinomyces* in our cultures shows but little color other than black. On media the color develops slowly and gradually to a dark gray, almost black. Some of the phenomena of pigment production and color may be explained, but in general the process is still obscure. For example, a darker pigment usually results in animals from the inoculation of fresh material from another animal than is the case if cultures are used. The next lighter shade is produced by inoculation with old, pigmented cultures, but color production is slower when young, unpigmented cultures are used for inoculation. Early pathologic lesions due to these parasites, like young cultures, rarely show pigment. The later in both instances is produced and grows more marked with age. Concentration undoubtedly has something to do with the apparent color of the pigment, for the harder the granule the darker the pigment appears to be.

Granule formation both in tissues and to a less extent, in cultures, is a property of all the pathogenic *Streptothricæ* with which we have worked. These granules vary considerably in consistency and color in the several species, but in the majority of instances they are made up of branching filaments with transformation products, which consist in irregular forms, crystals and unstainable detritus. The arrangement of the peripheral filaments may or may not be radial and there are various degrees of density of the mass. In two of our cultures (*S. canis* and *S. caprae*) there is less tendency to suppuration after inoculation in animals and the individual colonies have more the appearance of tubercles than in our other cultures. This difference has been pointed out by other observers. However, the lesions in our experimental animals were small; in the older lesions the type of the granule is not known, if we except the knowledge gained from the statements of the authors who described the parasites, the description being taken from the original lesions. The granules or colonies produced by the other cultures were in the majority of cases free in the necrosed, liguefied substance found in the various channels produced by these infections.

Club formation, in the lesions, in tissues and less frequently in cultures, is used as one of the points of differentiation between species of the organisms of this group. No doubt there is considerable variation in this respect under certain conditions, but the circumstances reported as surrounding club development are sufficiently varied and confusing to detract somewhat from what would otherwise be valuable for purposes of distinction.

Wright found club formation to be rather constant in original lesions, and observed it occasionally in certain cultures. In experimental lesions, it was also fairly constant, except in early lesions where clubs were sometimes absent.

Bostroem and others, working with species differing somewhat from Wright's organism in other particulars, also observed clubs both in lesions in animals and occasionally in cultures.

None of our cultures show definite clubs in culture or in experimental lesions in animals, although in several the terminal branches show some enlargement suggesting club formation (see illustrations). Our experimental animals were all killed within a shorter time after inoculation than were those of Wright, in which clubs were found.

Branching is similar in all of our cultures and is also similar to that recorded by most observers who have worked with this group of microörganisms.

The cultural characteristics of all of our strains have already been described. While there are variations in the reactions between some of these strains, they all appear to belong to one group of organisms, and if we analyze the literature carefully others, including the organisms of Wright and of Bostroem, may also be included in the group.

The following may be noticed if we take up the principal cultural characteristics comparatively as well as somewhat more in detail.

Surface growth **is considered to be poor in Wright's organism and is not very profuse in some of our strains, but in Bostroem's organism and in most of ours, while it may be slow, it does occur in a satisfactory manner and in some strains**

it may be luxuriant. There is but little tendency for surface growth to spread in any of the cultures, but on the other hand, it heaps up, as it were, giving raised colonies sometimes 1 centimeter above the surface of the media. (See plates.) This is also true with Wright's organism, where surface growth appears.

Wright first called particular attention to the character of growth in glucose-agar suspension cultures. In this medium with his organism, there is a narrow zone 5 to 10 millimeters below the surface where the colonies are very numerous but small, while lower down they are less numerous, but of larger growth. Surface growth is the rule in our cultures in this medium, and only occassionally a colony may develop in its depth.

Stab cultures in sugar-agar.—Growth with Wright's organism occurred in small nodules along the course of the needle, it did not penetrate the medium to any extent and did not grow on or near its surface.

The growth in our cultures occurs mainly upon the surface and upper portion of the track of the needle.

Anaërobiosis.—Wright considers his organism as an obligate anaërobe, a statement which is somewhat qualified in the details of his work. For example, in discussing the growth upon glucose-agar suspension media he states that the most profuse growth of the organism is in a narrow zone 5 to 10 millimeters below the surface of the medium and that this way may be "explained as the result of a stimulating action exerted upon the growth of the microörganisms by the presence of a small amount of oxygen which has penetrated into the medium from the surface." This oxygen requirement is further illustrated by the author when he states that "in sugar-agar suspension cultures, placed under anaërobic conditions, there is little or no tendency to form colonies on the surface."

Growth occurred along the course of the needle only in stab cultures on glucose-agar. It did not penetrate the medium and, on the other hand, did not grow on the surface. However, when discussing growth upon surface inoculations in slanted solid media, Wright found that surface growth was not luxuriant and in some of his strains no growth occurred even under anaërobic conditions. Again, Wright observed that "in general, growth appears to be as luxuriant in bouillon either under aërobic or anaërobic conditions." To judge from the above and other statements which might be taken from Wright's excellent monograph and *according to the standards used in this report* for the other members of the group, Wright's organism must be considered to be a facultative anaërobe.

In *bouillon* media there is some variation between the manner of growth of our cultures, but little which may be considered of value in the differentiation of species. The tendency in some of our cultures is toward a surface growth which may gradually separate and fall to the bottom, or settle on the sides of the tube. In other instances, the majority or all of the growth may occur at the bottom of the tube. The medium is not clouded, but in some cases it becomes darker, apparently because of the absorption of pigment from the organisms. There are no essential differences between our cultures in bouillon and those reported by Wright.

Potato, as is well recognized, is not a very satisfactory medium for comparative studies, excepting where the same set of media is used. Fairly luxuriant growth was obtained in every instance with our cultures on potato slants.[2]

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[2] The potato slants employed in this laboratory are made from selected potatoes treated and prepared according to the rules laid down by the committee of the American Public Health Association.

There was not much variation between the different cultures except in the color of the pigment and the appearances which have already been described. Potato proved itself to be a very unsatisfactory medium for Wright's organism. Most of his strains grow on it very poorly, and some of them not at all.

Litmus-milk is not a favorable medium for the differentiation of species. Growth takes place slowly, and with two strains the color is slowly discharged. No other appreciable changes occur in the medium excepting with cultures of "chalcea," in which a slightly acid reaction is produced.

The favorable influence of *sugar* and *glycerine* upon cultures of all strains of the group of organisms has been noted repeatedly. Sugar or glycerine containing media not only are the best in securing growth, but with all our species pigment production is more active in these media.

Pathogenic characters.—The pathogenic character of many varieties of this group of organisms in the human and animal economy is well established. However, experimental inoculations in animals have not given constant results in the hands of other investigators, and our experiments have been uncertain with all animals except monkeys. The details have already been described and it only remains to state here that lesions similar in their gross and histologic appearances to the original ones produced by these organisms, have resulted with each of the strains which we have studied, except with one of the strains of *S. Madurae* which has already been mentioned in this discussion.

CONCLUSIONS.

There is, in human pathology, a very important group of branching, filamentous microörganisms which logically belong to a single genus. The generic name is variously given as *Streptothrix, Actinomyces* or *Nocardia;* the last of these names is probably scientifically the most correct, but because of the present botanical confusion and uncertainty the first is here employed, because of its more general acceptance.

The following species to judge from our work and from a study of the literature are the most important and may be recognized as established. There are probably a number of others but the description of many of them are too imperfect to allow of their recognition.

S. actinomyces Bostroem, 1890.
S. actinomyces Wolff & Israel, 1891 and Wright, 1905.
S. nocardii.
S. eppingeri.
S. maduræ Vincent.
S. capræ Silberschmidt.

The disease caused by infection with these parasites is properly named streptothricosis, with actinomycosis and nocardiosis as synonyms. Other names, such as lumpy-jaw, madura foot, mycetoma, etc., should be considered more as describing anatomic location rather than as designations relating to any special or specific cause of infection. Mycetoma might well be taken as the correct name for the group of infections if a strict interpretation of rules of nomenclature is followed, but usage renders it perhaps more desirable to retain the name as representing

Streptothricosis pedis. If mycetoma is to be considered in any more comprehensive light than this, it should become another synonym for streptothricosis. It should not be considered a disease caused by organisms other than *Streptothricæ.*

PART II.

STREPTOTHRICOSIS.

SYNONYMS.—Actinomycosis, Nocardiosis.

DEFINITION.—An infectious disease of man and animals caused by one or more species of *Streptothrix.* It is characterized anatomically by a peculiar, low grade of inflammation, usually confined to one part of the body, but in rare instances assuming the proportions of a general infection. The inflammatory process usually is accompanied by suppuration of a certain kind; the discharges contain granules made up principally of colonies of *Streptothrix.* The general picture of chronic inflammatory disturbance is seen clinically, and enlargement, suppuration and the presence of the causative organism in the lesions is observed locally.

HISTORY.—The history of *Streptothrix* infection is shown in the review of the literature given in Part I. In general it may be stated that the disease has probably long been recognized and frequent references are made in older medical literature to conditions which presumably were due to infection with these microörganisms. According to Rivolta, Trutto discussed the condition among cattle in Italy in 1785 under the name of "Krotenkrankheit." The colonies of the organisms were more or less accurately described by Langenbeck (1845), Sir T. Smith (1855), Lebert (1848), Rivolta (1868), Robin (1871), Heller (1872), Perroncito (1875), and others (see Ackland). Mention of the anatomical form of the disease generally described as mycetoma or Madura foot are also quite old, the principal authors being: Kämpfer (1712), Heynes (1806), Brett (1840), Gill (1842), Godfrey (1844), Colebrook (1844), Gunther (1844), Eyre (1848), Bollingol (1855), Eyre (1860), Collos (1861), Bidie (1862), Hirsch (1868 and 1886), Coquerel (1866), and many others (see *This Journal, Sec. B.* (1907), **2**, 487). Of these observers Colebrook (1850), Bollingol (1855), Coquerel (1866), Maxon and Hogg (1870), Bristowe (1871), Berkeley (1876), and others probably saw and in a few instances partially described the organisms present in the lesions. However, the really important history of *Streptothrix* infections dates from Vandyke Carter's work (1859–1874). This author described and illustrated the parasites in many cases of the foot (Madura foot) type of the infection. Bollinger and Marz (1876) first accurately described and named one of the parasites causing the disease known as lumpy-jaw in cattle. The next epoch in the history was due to an article by J. Israel (1878) who was the first to describe the disease and parasite in man in locations other than the foot (Madura foot) and hand, the infection in these places already having been described by Carter and others. Israel's work was followed by that of Ponfick (1879) with strong evidence as to the identity of the disease in man and animals. From the year 1876 the literature accumulated rapidly and the infection was reported for man and animals from widely varying locations and countries.

Bostroem (1890) contributed the first thorough and exhaustive laboratory study of the microörganisms and this work was followed a year later by an equally exhaustive treatise on the same subject by Wolf and Israel. The organisms described by Bostroem on the one hand and by Wolf and Israel on the other, although isolated from apparently similar diseases, showed certain morphologic and biologic differences which led to much discussion during the next few years. Organisms corresponding to the descriptions of both these pioneer observers continued to be mentioned in the literature, each investigator maintaining his organism to be the true cause of the disease.

In 1888 Nocard cultivated and quite accurately described a *Streptothrix* as the cause of a disease locally termed *farcin de boeuf* of cattle in Guadalupe; Nocard's organism seemed to be of a different species from either Bostroem's or Wolf and Israel's. Eppinger (1890) cultivated and accurately described another species of *Streptothrix* as the cause of a brain abscess and "psuedotuberculosis" in a man. Vincent (1894) first satisfactorily cultivated and described a *Streptothrix* as the cause of mycetoma or Madura foot and his organism seemed to have certain characteristics showing it to be specifically different from any of those previously described.

Foulerton (1899–1907) gave descriptions of several new species of the parasites and has brought out the most thorough and exhaustive consideration of the whole subject with which we are familiar. Wright (1905) contributed a most complete and exhaustive study of the biology of the Wolf and Israel variety of this organism. The work of bringing all this group of similar organisms together in a single genus is largely due to the researches of Rossi Doria, Petruschky, Foulerton and several other recent writers, particularly of the German and French observers.

In this article we have shown conclusively that Eppinger's organism isolated from clinical actinomyces on several occasions is identical with *S. freeri*, which is one cause of Madura foot in the Philippine Islands. Very little is known regarding *Streptothrix* infections in this Archipelago. Our records show two cases in which *Actinomyces* was the etiologic factor in human disease, and several infections of cattle have been observed in the islands. One case of the Madura foot type of the disease has been seen.

ETIOLOGY.—*Predisposing causes,* for this disease, except in a few instances, have not been sufficiently studied to make a satisfactory estimate of their influence.

The *geographic distribution* is very wide, but no very large series of cases have been studied by any one observer. Collections of such series have been made in America, Germany, France, England, Russia, Switzerland, and in the British colonial possessions. The most frequent incidence is found in certain parts of the Tropics, particularly in India, but, as has been pointed out by Ackland, the disease may be overlooked in a community for a long time until special attention is called to its prevalence.

According to available statistics the infection is more frequent during young, adult life, but cases have been reported in children and in old people. Males are much more frequently affected than females—295 males to 110 females being given in Leith's statistics, and 65 males to 36 females in Ackland's.

Race, nationality, residence, overcrowding, climate, occupation, and physical condition, to judge from available statistics, seem to exert but a minor influence on the spread of the disease, although a more careful study of a large material may show some of these to have greater significance.

General environment and *mode of living* would naturally be expected to have considerable influence as predisposing factors, particularly in determining the part of the body involved. For example, the Madura foot type of infection is most common among people who go barefoot, it being largely a wound infection.

Streptothricæ are the specific, causative agents of the infection. They have already been considered in Part I of this report, and only a brief summary will here be given.

SYNONYMS.—*Actinomyces, Nocardia, Oöspona, Chenaphe carteri.*

DIAGNOSIS of these organisms is made from morphologic and biologic considerations. They are branching, filamentous organisms, which develop slowly into colonies made up of the branches and their "transformation products." These colonies vary in color, size and consistency, and when stained show various changes in different portions. The filaments at the periphery are usually intact, with or without club formation, and the terminals may or may not be radially placed. Toward the center of the colony, or granule, irregular forms, such as coccus- and bacillus-like ones, are found, together with crystals and nonstaining detritus.

The majority of these organisms may be cultivated on artificial media, where they show various but characteristic biologic properties. That some of them are pathogenic tissue parasites is shown by their action on laboratory animals.

Morphologically these parasites are rather closely related to some of the branching bacteria. The young filaments vary in width from 0.5 to 1 μ and in length from 5 to 20 μ or more. They usually stain homogeneously, and in some strains taken from lesions they are acid-fast to the

Ziehl-Neelsen-Gabbett method. In older forms the segments are often broken, the sheath-like substance not showing either in fresh or stained specimens. The breaking up of the filaments produces great variety and size of irregular forms; some of these may appear to be very much like bacteria, but their true nature is easily established by laboratory methods. The majority of these organisms may be stained by the aniline dyes, all show Gram positive characteristics to a greater or less degree, and several are as acid-fast as is the tubercle bacillus.

Biologically certain species—both saprophytic and pathogenic—are widely distributed in nature. They have been found on food stuffs—particularly cereals—in water, air, soil, etc. Zoölogically they are found in some insects and several animals, and in man. Cattle are the most frequently infected of the animals, but rarer instances of the disease have been reported for other species.

Cultivation of these organisms is probably possible with all species, although several authors have reported failures, and all observers have noted the difficulty of obtaining a culture from the lesions in animals. However, when adaptability to artificial media has once been secured, no very great difficulty is found in keeping the culture. In general, it may be stated that these organisms grow slowly on artificial media, but that the cultures show most positive characteristics in the majority of instances. In all there is a tendency to "pile up" on the medium rather than spread over the surface. Pigment production of various shades is a very common property, and this is more marked as a rule in glycerine or glucose containing media.

Resistance to physical, chemical, and other agents by these organisms is rather great if we consider them to be non-spore bearing parasites, but this resistance is not sufficient to permit us to consider that true spore formation is present as it is understood for bacteria.

PATHOGENIC CHARACTER.—The pathogenicity of several species of *Streptothrix* has recently been demonstrated by different workers, according to the accepted bacteriologic rules governing such decisions. Other members of the group appear to be saprophytes in that they do not produce lesions in animals by the usual methods of procedure. There is also considerable lack of uniformity in the results of animal experiments with nearly all the pathogenic strains. However, working with monkeys, our results have been more uniformly successful than those reported by other observers, or than our own results with other laboratory animals. The pathogenicity of this group of organisms seems to be influenced to a certain extent by the same conditions which produce changes in the virulence of bacteria. Not only may the virulence of some of these species be increased by passage through susceptible animals, but with the increased virulence differences in cultural results may be noticed. These are shown principally in greater difficulty in securing growth, in a slower growth on artificial media and sometimes in slight changes in the color and quantity of pigment production.

Some of the so-called saprophytic species may in reality be found to be pathogenic, when improved technique is used.

Modes of transmission.—Although experimental evidence is still far from satisfactory regarding modes of transmission, it seems to be entirely reasonable to assume from the known biology and the available evidence, that transmission may take place both directly and indirectly. So far as we are aware, no positive examples of direct transmission from person to person have been reported, but that such infection does not take place in localities with high incidence of the disease, seems probable. Rather convincing evidence of indirect transmission through the agency of food-stuffs, water, etc., has been furnished by several observers. Several authors whose work has already been reviewed, have shown that pathogenic species may be isolated from water, air, soil, and food-stuffs and the history of many of the reported cases indicates infection from some such source. The frequent presence of the infection in the lower animals must not be forgotten in considering the manner of transmission of the parasites.

Infection probably takes place in two general ways, first, by direct or wound infection, as is shown in many cases by the history of injury before the development of the symptoms of the *external* forms; and secondly, infection by way of the respiratory or gastro-intestinal tracts, which is shown in many of the *internal* forms of the disease.

Species.—The number of species important in this disease is probably a considerable one. Those which we have been able to recognize from the literature and our own work are given in Part I.

It seems probable that all the species have not, as yet, been discovered and that some, which have been described, are specifically different from the ones mentioned here.

PATHOLOGY.—In general the morbid changes found in this disease are those of a peculiar, low-grade, chronic infective process. Anæmia, atrophy of tissues, and mild, chronic degenerations of parenchymatous organs are present. The special pathology depends somewhat on the part of the body involved and on the extent of this involvement. The streptothritic unit, as it were, is a granule which is usually surrounded by a zone of peculiarly appearing suppuration, and this in turn by an area of inflammation characterized by connective tissue proliferation and cell infiltration. Cells of the usual character are found, with a relative increase of fixed tissue cells and occasionally a giant cell. In other instances the suppurative zone is absent and the streptothritic unit takes on more the general and histologic appearance of a tubercle. In fact, the whole morbid process of *Streptothrix* infections resembles more or less closely that produced by *Bacillus tuberculosis.* Tissue destruction often spreads by means of continuity, but more usually by intercommunicating channels running in various directions. These channels contain the broken down tissue and granules made up of colonies of the infecting organism. Few tissues escape the destructiveness of the *Streptothrix,* but it appears to be more active in the connective tissues, bones, and mucous membranes. However, practically every organ and tissue of the body has been involved. The disease spreads through the body in at least two ways, by directly continuing along the tissues, in which case the area involved is rarely great, and by metastases through the blood vessels, when the infection may be so great as fairly to be considered a general infection.

The character of the morbid process suggests that the minute action is toxic in character, although if such is the case, the toxin must act very slowly. The lymphatics near a diseased process may be enlarged, but are rarely found to be broken town or to contain the microörganism.

SYMPTOMS.—The clinical manifestations of *Streptothrix* infections are essentially those of a slowly developing, chronic inflammatory process. They vary much with the location of the lesions and further complications are secured by the presence of mixed infections which are frequent when the disease attacks regions of the body exposed to bacterial invasion. In many instances, where the lesions are located in the internal organs such as the liver, definite clinical manifestations do not occur and unless the infection spreads, its nature in all likelihood is not recognized during life.

When the lesions are located externally, or in places where the discharges reach the surface of the body, the nature of the infection should be suspected from the appearance of the wound and the character of the discharges; on the other hand, it may be generalized, manifest itself in an acute course and be difficult to distinguish from a pyæmia of other etiology.

The *incubation* period varies between wide limits, and as given by authors may be from a few days to more than two years. The onset is usually gradual, by the slow development of the lesions.

The following clinical varieties may be recognized:

Generalized streptothricosis.—This form of infection has been noted by several observers. It occurred 9 times in Ackland's 109 cases. This type usually begins in a local lesion and is transmitted through the blood vessels. In the majority of instances, it occurs in mixed infections with bacteria, but cases in which no bacteria were present have also been reported. Several species of the organisms causing these general infections have been found. This type is generally acute or subacute clinically and the symptoms as given by various authors are similar to septicæmia or pyæmia from other causes. Extensive lesions may occur in practically every organ and tissue of the body. The diagnosis is only made by laboratory methods, the prognosis is bad and treatment unsatisfactory.

Thoracic streptothricosis.—The organs of the chest, particularly the lungs and pleuræ are most frequently involved in this disease. It occurred 65 times in 257 cases reported by Duvan and 29 times in Ackland's 109 cases. The clinical symptoms in the lungs and the physical signs may resemble a chronic tuberculosis or severe bronchitis and the pleural involvement may consist of chronic, adhesive pleuritis or more often of empyæma. Unless there is perforation of the chest wall or metastases, the clinical manifestations in these types show nothing characteristic of the disease and the true nature of the infection can only be determined by laboratory methods. Streptothricosis of the heart and mediastinum have been reported, and Ackland notes nine cases involving the œsophagus.

Abdominal streptothricosis, including all the organs of the abdominal and pelvic cavities, have been reported by various observers. The liver and gall bladder suffer most often. Involvement of these viscera occurred forty times in Duvan's series and thirty-three in Ackland's. The appendix is quite frequently involved and in some instances is the primary seat of the lesions.

Other lesions are found in the mesentery, intestine, rectum, spleen, bladder, prostate, testicle, kidneys, and abdominal wall. In none of these types are there any characteristic clinical manifestations which differentiate this infection from other chronic inflammatory conditions of tuberculous or other etiology in the same locations.

Cerebral streptothricosis includes involvement of the brain, cord, meninges, and nerves, as well as the other tissues in these organs. The central nervous system was involved 19 times in Duvan's 257 and 5 in Ackland's 109 cases. Several different species of the organisms have been found in these lesions, that of Eppinger being the principal one. This species, as has been shown in Part I of this report, is identical with *S. freeri* which caused the mycetoma in our case. The reported cases show no characteristic symptoms in these types of infection.

External streptothricosis may involve any of the external or contiguous tissues, including the mouth and jaw, neck, skin, and subcutaneous tissues, conjunctiva, nose, and extremities. "Lumpy-jaw" or "big-jaw" is one of the most frequent of these various types; mycetoma, Madura foot or *streptothricosis* pedis is a very common tropical type and others involving many anatomical locations are frequently encountered. Practically all described species of the genus of the organism have been found at one time or another in external streptothricosis, and there does not appear to be much variation in the clinical picture because of any special species or variety. The clinical manifestations of external streptothricosis are rather characteristic. The peculiar, crater-like skin lesions of a chronic character leading through ramifying channels, through which is discharged the peculiar, oily, pus-like substance containing granules, makes a rather constant and characteristic picture. As we have already stated, mycetoma or Madura foot is best classified here as the clinical type of *Streptothricosis pedis,* because it may be caused by several if not any of the species of this genus and the clinical manifestations are practically the same in all cases. The special symptoms of this type are well known and have already been discussed in this report.

Miscellaneous types of streptothricosis may be mentioned, such as involvement of the conjunctiva, bones, ear, nose, intercostal spaces, etc. Their only peculiarities are in the anatomical locations of the lesions.

DIAGNOSIS.—The diagnosis of *Streptothrix* infections is made clinically by the character of the exposed lesions and discharges and by laboratory methods. Obviously, the common and frequent involvement of internal organs is rarely recognized except by microscopic examinations at operations or at autopsy. The thoracic types may be determined by microscopic and bacteriologic studies of the sputum or aspirated fluid from the pleural cavities. It is generally stated by competent observers that these types are frequently overlooked, even in sputum examinations and it is not improbable because of the acid-fast properties of some of the organisms that they may occasionally be mistaken for the tubercle bacilli. The resemblance may, at times, be quite close. In some of our experimental lesions the similarity has been striking. The microscopic examination of material from exposed lesions often requires some patience and care to enable the observer to find the organisms; unless a granule is encountered, when, of course, the determination is easy. Inasmuch as some other closely related organisms such as *Oïdia, Leptothrix,* and *Cladothrix* may cause somewhat similar lesions, *Streptothricæ* should not be diagnosed positively without careful microscopic study of the organisms present in the lesions.

PROPHYLAXIS.—From what we know of the distribution of the organisms of this disease and the mode of transmission and the prevalence of certain anatomical types, prophylaxis should consist in guarding against wound infection and generally by care in food and drink. In the Tropics most of the types consist in local foot or other skin wound infections, which should be guarded against by wearing shoes and by promptly treating skin wounds and abrasions according to antiseptic methods.

PROGNOSIS.—The prognosis depends to a considerable extent upon the location and extent of the lesions. The general infections and those of the internal organs almost always end fatally. The external types are much more amenable to treatment and the mortality is small.

According to the statistics of Duvan, and Poncet and Berard who analyzed 257 cases, the mortality was as follows: Skin, 2.3 per cent; face and neck, 10; jaw and temporal region, 30; abdominal cavity and intestine, 65; thoracic, 85; liver, 100, and brain and spinal cord, 100 per cent. The mortality in mycetoma, under proper treatment, is very small. The course of the disease is usually chronic, but it may be general

:hrix capræ Silberschmidt.	Streptothrix freeri.
Our culture	Our culture.
Short filaments resembling ba coid forms; occasionally lon ing branching but no club f	Long, branching filaments, 2 to 7 μ in diameter. Transverse segments are shown of various length from coccoid to 10 μ in length. Branching occurs as lateral hyphæ developing from the segments. The filaments have a definite wall. Spores have not been observed. Coccoid and club-like forms present in certain medium.
Cultures from 2 weeks to 2 mo Ziehl-Neelsen method show m tions, giving the organism short, plump bacilli. Gram- staining.	Culture from 5 days to 2 months stained by Ziehl-Neelsen method show many acid-fast portions. The organism is Gram-positive.
Growth appears in 2 or 3 days colonies; medium remains m so well nor does it produce t medium that it does on th media.	From 2 to 3 days' growth appears as smooth, glistening colonies which later coalesce and produce a delicate pink pigment; medium remains moist.
Growth appears after 2 days a white colonies which later c growth a moist, mealy appea brownish color.	Growth after 3 to 4 days at first as small, whitish colonies; these gradually take on a delicate pink color; later as the colonies develop they become umbilicated and coalesce forming a heaped-up growth and produce a burnt-ocher color.
Similar to glycerine-agar..........	Similar to glycerine-agar.
Appear after 3 days as sligh which soon assume a light-bro	Do.
Colonies develop on the surfac and later form a surface m forms at the bottom of the mains clear.	Growth appears after 3 days as flat particles on the surface of the medium; these produce in time a delicate pink color; as growth proceeds a granular mass collects in the bottom of the tube; this mass is more or less coherent.
Very slight growth; no pigme	Very slight growth; no pigment; no clubs.
Pathogenic for guinea pigs an cutaneous and intraperitonea	Pathogenic for guinea pigs and monkeys by intraperitoneal injections.

and acute and general infection may take place during the course of a chronic localized type of the infection.

Complications.—While streptothricosis may be found together with a number of other diseases, or may develop its symptoms as sequelæ of other diseases, the principal direct complications are those due to mixed infections of bacteria. Several of the pathogenic bacteria have been found associated with *Streptothricæ* in lesions and the course and outcome of the disease is influenced accordingly.

Tuberculosis, because of its close clinical relation to streptothricosis and the frequent lung involvement of both organisms, has led to confusion in some of the reported cases.

Treatment.—The varieties of treatment most useful in this disease are general, as well as local surgical intervention if cause is indicated and a combination of all of these methods may be necessary. Potassium iodide administered in large doses over a long period of time is generally admitted to have a favorable influence on the course of the disease and complete cures have been reported from this method of treatment. Local measures consist in antiseptic dressings and the use of the Roentgen rays. Surgical measures consist in drainage, removal, or amputation according to the location and extent of the lesions. A combination of all three forms of treatment would suggest itself as offering the most favorable opportunity for recovery.

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ILLUSTRATIONS.

(Colored photographs and photomicrographs are by Charles Martin, photographer, Bureau of Science, Manila.

PLATE I.

FIG. 1. Cultures of *S. eppingeri* from Foulerton's case.
2. Culture of *S. eppingeri* from original strain.

PLATE II.

FIG. 3. Culture of *S. maduræ* from Foulerton.
4. Culture of *S. maduræ* from Strong's culture.

PLATE III.

FIG. 5. Culture of *S. maduræ* from Vincent's strain.
6. Culture of *S. actinomyces* from Binot.

PLATE IV.

FIG. 7. Culture of *S. nocardii.*
8. Culture of S. *capræ.*

PLATE V.

FIG. 9. Culture of *S. canis.*
10. Culture of *S. freeri.*

PLATE VI.

FIG. 11. Culture of *S. freeri*, showing structure of individual colony.
12. Culture of *S. chalcea.*

PLATE VII.

FIG. 13. Section from experimental lesion in monkey produced by inoculation with culture of *S. eppingeri*, × 60.
14. Unstained smear preparation from culture of *S. eppingeri*, × 600.
15. Smear preparation from culture of *S. eppingeri* stained by gentian violet, × 800.
16. Section from experimental lesion in mesentery of monkey produced by inoculation with culture of *S. eppingeri*, × 600.

PLATE VIII.

FIG. 17. Smear preparation from culture of *S. maduræ* stained by gentian violet, × 400.
18. Same as No. 17, × 600.
19. Section from experimental lesion in monkey produced by inoculation with culture of *S. maduræ*, × 60.
20. Smear preparation from culture of *S. canis* stained by gentian violet, × 650.
21. Same as No. 20, × 650.

PLATE IX.

FIG. 22. Smear preparation from culture of *S. maduræ* (Strong's culture) stained by gentian violet, × 500.

23. Same as No. 22, × 700.

24. Same as No. 22 excepting that the preparation is unstained, × 500.

25. Smear preparation from culture of *S. actinomyces* (Pasteur Institute) stained by gentian violet, × 700.

26. Section from experimental lesion in monkey produced by inoculation with culture of *S. maduræ*.

PLATE X.

FIG. 27. Smear preparation from culture of *S. capræ* unstained, × 600.

28. Section from experimental lesion in monkey produced by inoculation with culture of *S. actinomyces*, × 600.

29. Smear preparation from culture of *S. actinomyces* stained by gentian violet, × 650.

30. Smear preparation from unstained specimen of *S. actinomyces*, × 650.

PLATE XI.

FIG. 31. Smear preparation from culture of *S. capræ* stained by gentian violet, × 650.

32. Section from experimental lesion from monkey produced by inoculation with culture of *S. capræ*, × 600.

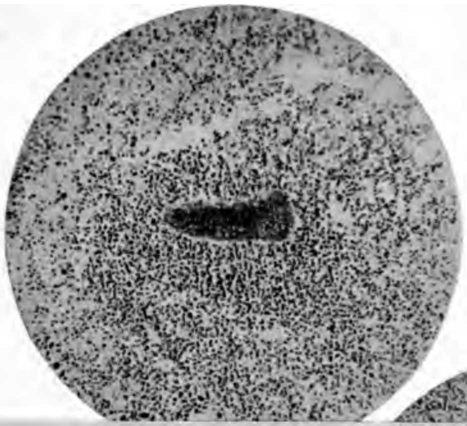
33. Smear preparation from culture of *S. capræ* stained by gentian violet, × 1100.

34. Section from experimenal lesion in monkey produced by inoculation with culture of *S. capræ*, × 60.

PLATE XII.

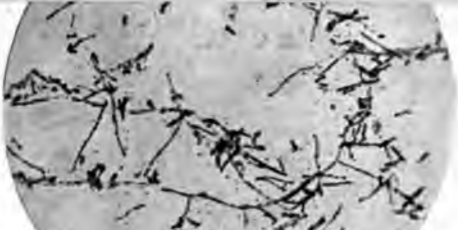
FIG. 35. Smear preparation from culture of *S. chalcea* stained by gentian violet, × 850.

36. Smear prepration from cultures of *S. nocardii* stained by gentian violet, × 850.



Plates I to VI inclusive are colored reproductions of cultures. As it was impossible to complete them in time, they will be included separately, for binding, in a subsequent number of this Journal.

FIG. 14.



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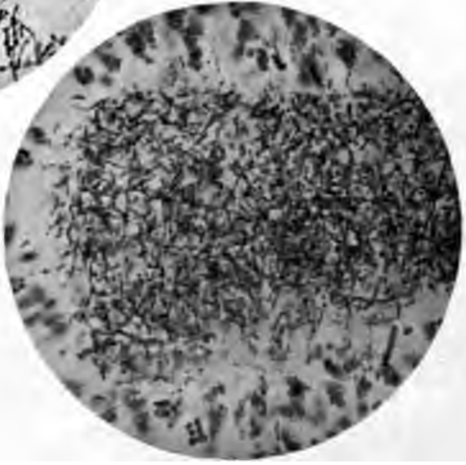
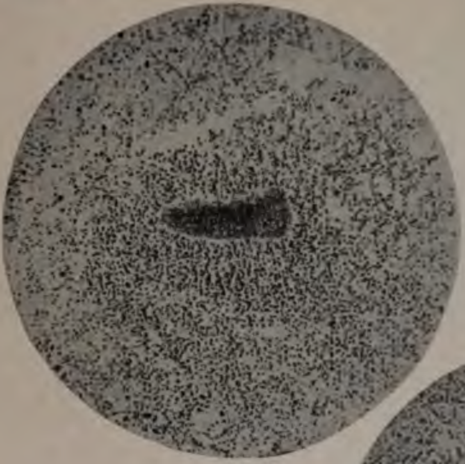


FIG. 16.

PLATE VII.



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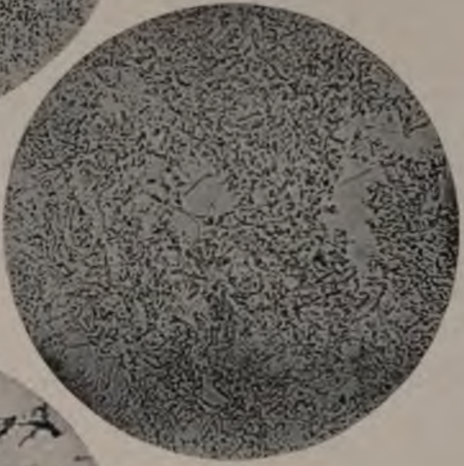

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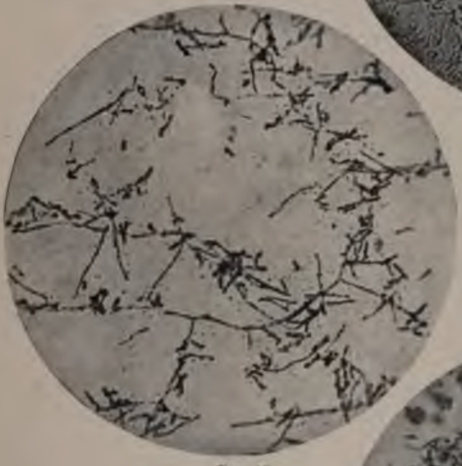


FIG. 15.

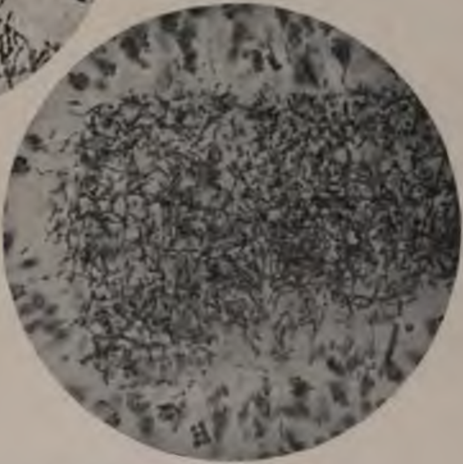
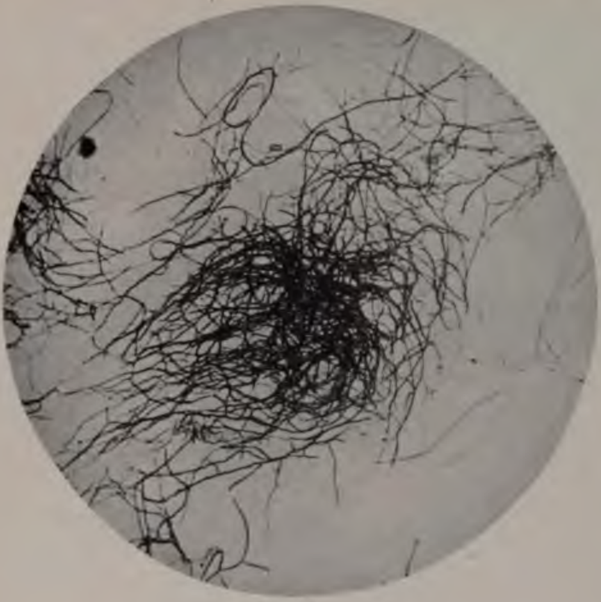


FIG. 16.

PLATE VII.



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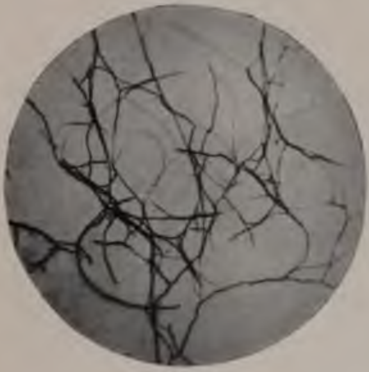

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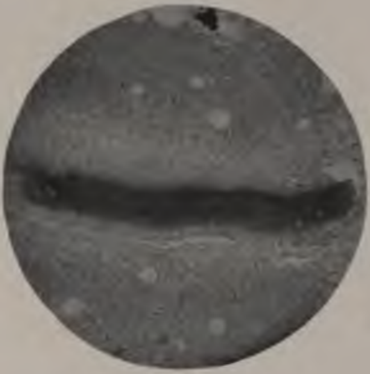

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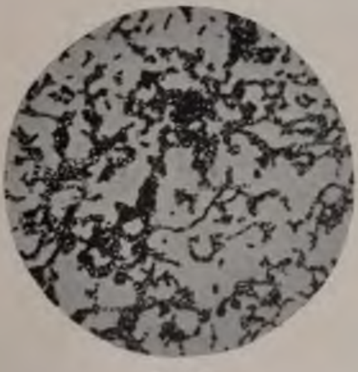

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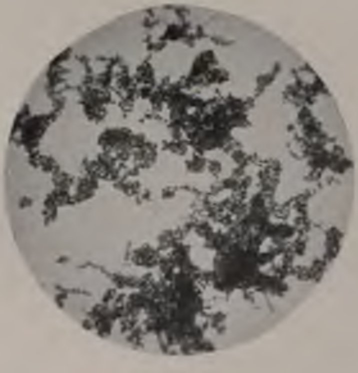
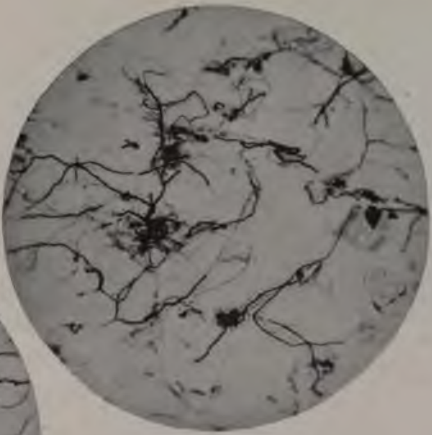


FIG. 21.

PLATE VIII.



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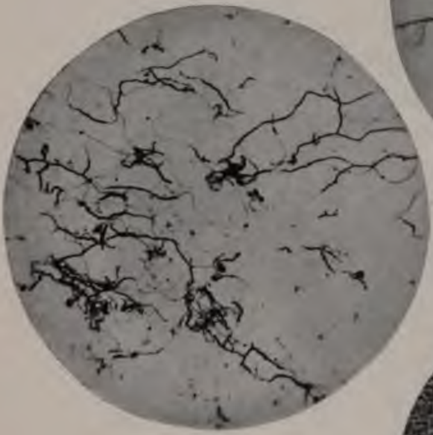

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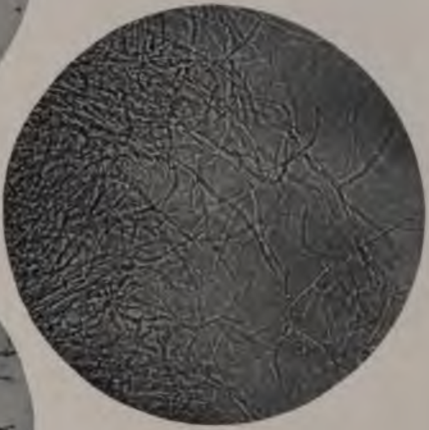

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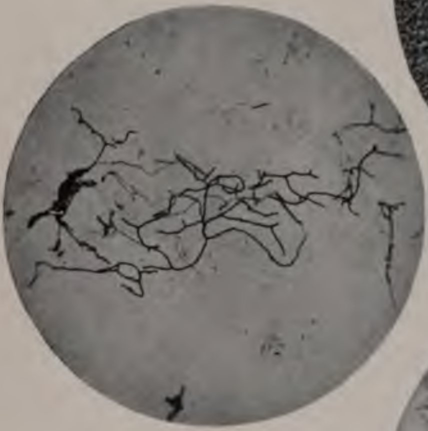

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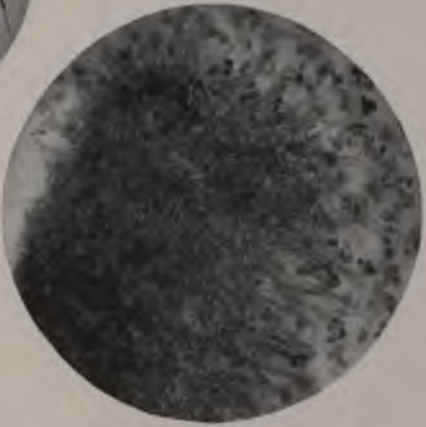


FIG. 26.

PLATE IX.

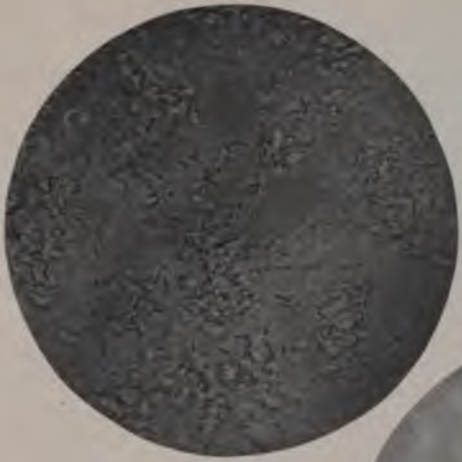


FIG. 27.

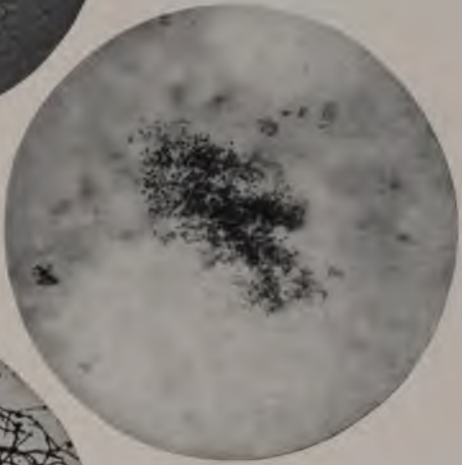
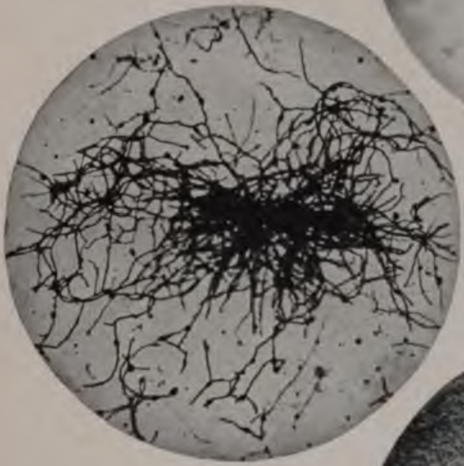


FIG. 28.



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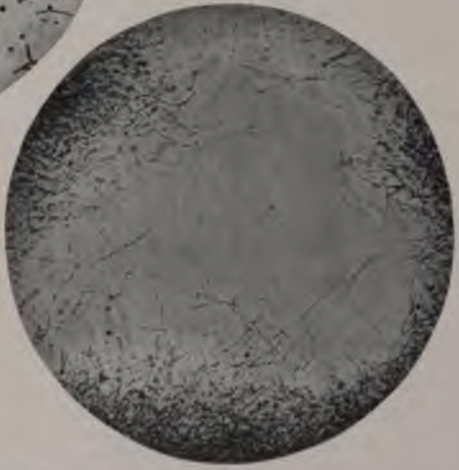
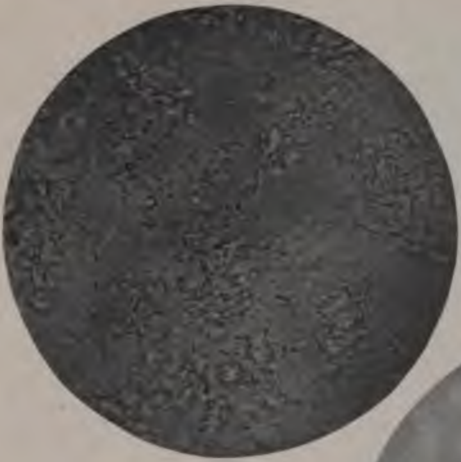


FIG. 30.

PLATE X.



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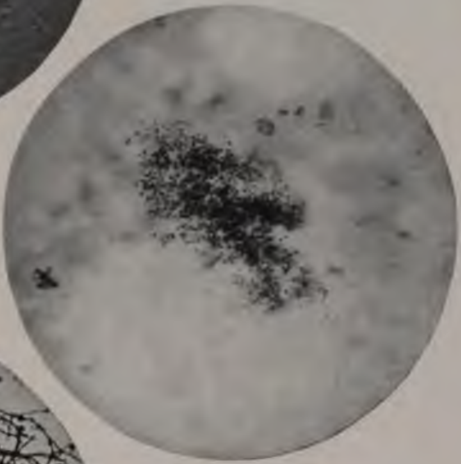

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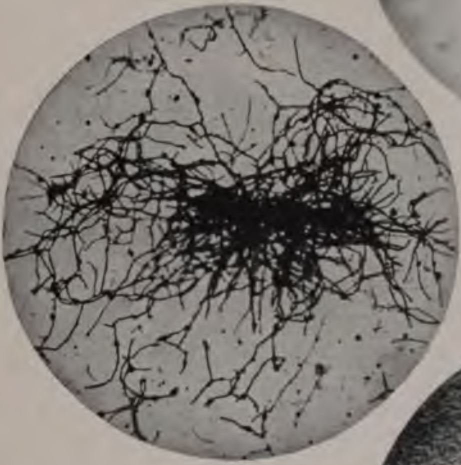

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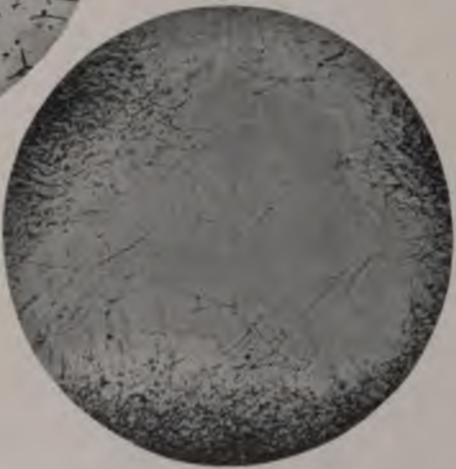
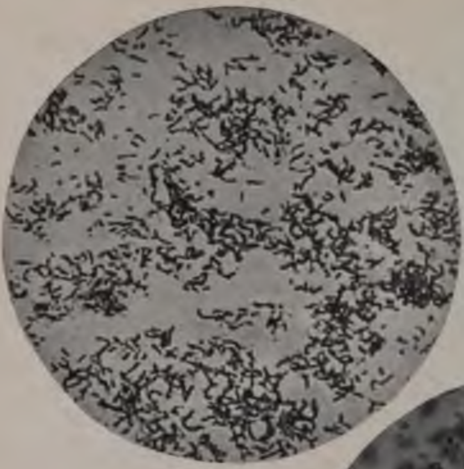


FIG. 30.

PLATE X.



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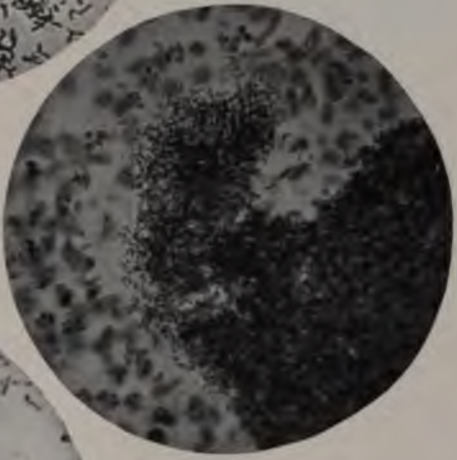

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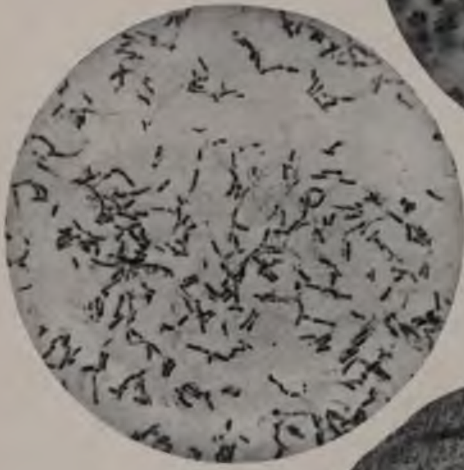

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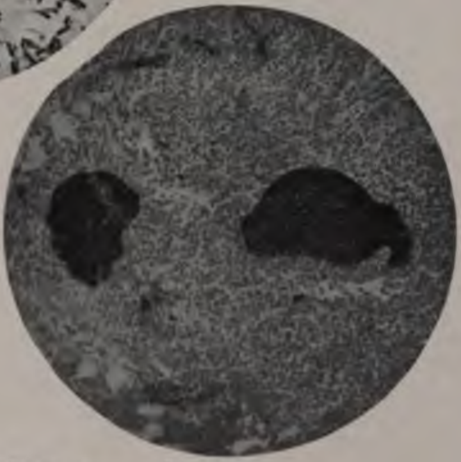

PLATE XI. FIG. 34.

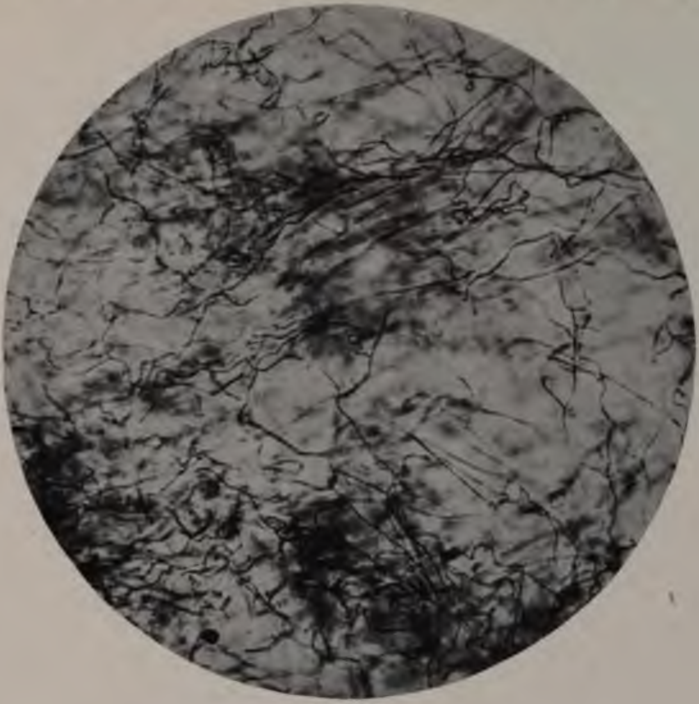

FIG. 35.

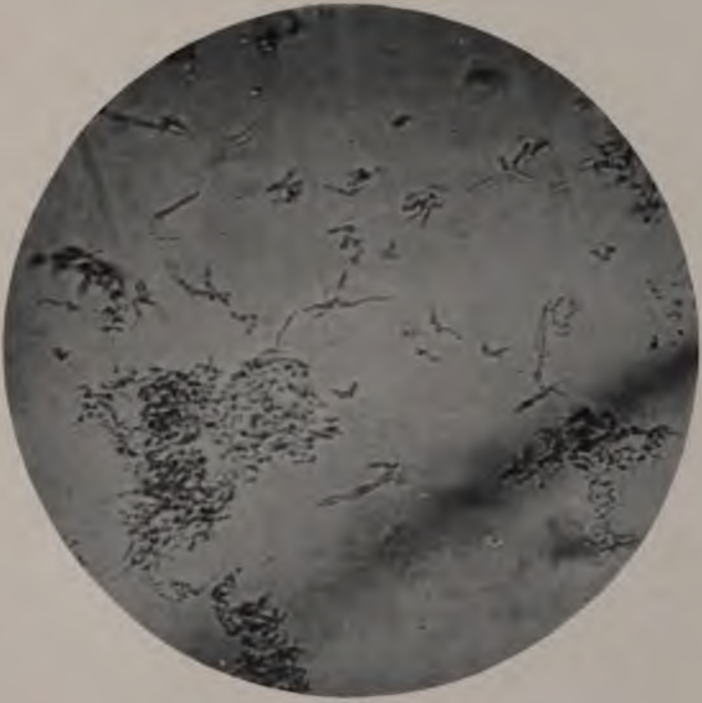

FIG. 36.

PLATE XII.

TRICHOCEPHALIASIS.

(WITH A REPORT OF FOUR CASES, INCLUDING ONE FATAL CASE.)

By W. E. MUSGRAVE and M. T. CLEGG, with a
bibliography by MARY POLK.

(From the Biological Laboratory and the Library, Bureau of Science.)

OUTLINE.

- INTRODUCTION.
- CASE REPORTS.
- LITERATURE OF THE DISEASE.
- TRICHOCEPHALIASIS.
  - Synonyms.
  - Definition.
  - Etiology.
    - Contributing causes.
    - Trichocephalidæ (by P. E. Garrison).
      - General discussion of the genus.
      - Trichuris trichiura.
      - Modes of transmission.
        - Direct.
        - Indirect.
          - Water.
          - Food.
          - Insects (flies, etc.).
          - Soil.
          - Dust, clothing.
          - Air.
          - Animals.
- TRICHOCEPHALIASIS—Continued.
  - Etiology—Continued.
    - Trichocephalidæ—Continued.
      - Pathogenesis (parasitism).
        - General.
        - Manner of infection.
  - Pathology of the disease.
  - Symptoms.
    - Incidence.
    - Clinical varieties.
      - Intestinal.
      - Appendicial.
      - Mild.
      - Severe.
  - Trichocephaliasis of animals.
    - Diagnosis.
    - Prognosis.
    - Prophylaxis.
    - Treatment.
    - Bibliography.

INTRODUCTION.

Our own experiences and a careful review of the literature of whipworm infections, convinced us that the subject has much more importance in human pathology than is generally assigned to it.

For this reason we have decided to publish four of our cases in detail, review the most important articles in the literature and then discuss the question of trichocephaliasis in monographic form with special reference to the disease-producing powers and clinical manifestations of infection with these parasites.

While it is true that the majority of investigators who have published the results of original work have attributed pathogenic properties to these parasites, and although these observations are supported by such authorities as Seifert, Stiles, Metchnikoff and others, to-day the majority of text books on medicine barely mention these infections and in general state that they are of little or no importance from a medical standpoint.

CASE REPORTS.

CASE I.—*Trichocephaliasis with severe progressive secondary anaemia followed by death; autopsy.*

L. G. N., male Filipino, 24 years of age, was admitted to St. Paul's Hospital August 9, 1908, died September 16. *Family history:* Father and mother are both living and in good health; two brothers died of smallpox. *Previous illness:* As a child the patient had chickenpox, a few mild attacks of "malaria," and five years ago suffered from an abscess of the parotid gland. *Present illness:* Three weeks before admission the patient began to feel dizziness, weakness, slight fever in the afternoons and ringing in the ears. This condition gradually grew worse and about ten days before admission he noticed beginning œdema of the ankles, hands, and face.

On admission the patient complained of shortness of breath, great weakness, ringing in the ears, palpitation of the heart, nausea, lack of appetite, dyspeptic symptoms and slight diarrhœa.

Examination.—The patient is a rather large, well-developed Filipino with marked œdema of the extremeties and face, marked pallor of the mucous membrane and rapid, shallow respiration. The circulatory system appears normal, except for a slight hæmic murmur heard at the apex of the heart and an increased pulse rate to 110, when the patient is in an upright position.

Blood examination as follows: Red blood cells, 1,800,000; leucocytes, 10,000; hæmoglobin, 20 per cent. Differential count: Mononuclear cells, 65 per cent; polynuclear cells, 30 per cent; transitional, 5 per cent. There are no nucleated red blood cells and but a moderate poikilocytosis. No eosinophile cells are present in a count of 500.

Respiratory system, negative. *Alimentary system* shows the following changes: Lips and other mucous membranes extremely pale, tongue large and flabby with a dark, almost black, streak down the center. Nothing abnormal is found in the abdomen, excepting a slight accumulation of fluid; the liver is slightly enlarged; the spleen is not palpable. The examination of the stomach contents shows no abnormality; examination of the stool after a saline cathartic shows enormous numbers of the ova of *Trichuris trichiura.* The urine is normal by chemical and microscopic examination. *Nervous system:* There is no pain, and the reflexes are normal. *Locomotor system:* Œdema and considerable flabbiness of the muscles are the only abnormalities noted. *Cutaneous system:* The skin appears normal and there is no enlargement of the superficial lymphatics. The patient's condition grew gradually worse from the time of admission with accentuation of the following symptoms: Œdema became general and progressed until death; the anæmia was also progressive, and the same general character of blood picture was maintained until the end. A count made a few days before death showed the following: Red cells, 844,000; hæmoglobin, 18 per cent. At this time there were still no nucleated red cells and no eosinophile cells to be found. Nausea, from which the patient suffered upon his admission, became more constant and toward the end vomiting was a very distressing and unmanageable symptom. The nervous and mental symptoms became more marked and during the last week of illness there was active delirium. The patient finally died of asthænia.

There were no hæmorrhages at any time and no severe diarrhœa. Repeated examinations of the stool always demonstrated very large numbers of *Trichuris* eggs. The temperature was practically normal throughout the course of the disease. Three separate attempts were made to dislodge the parasites, which were the only discoverable cause of the anæmia, the following substances being used for this purpose: Thymol in doses of 8 grams on two occasions and the well-known eucalyptus-castor oil and chloroform mixture on one occasion. A few *Trichuris* were obtained with two of these treatments, about 15 or 20 in all being secured. The stool from the third treatment was unfortunately destroyed without examination. Other treatment administered consisted in stimulation and in attempts to build up the nutrition.

Autopsy was performed one hour after death by Dr. Gilman and his report of the findings is as follows:

Body of a sparely nourished Filipino 157 centimeters long; rigor mortis absent; body still warm; pupils moderately dilated; equal; distinct yellowish tinge of sclerae; the entire body has a yellowish tinge. There is no general glandular enlargement; abdomen flat; no scar on penis. Shins clear.

Subcutaneous fat is present in good amount, is of a lemon-yellow color, more brilliant than normal. Muscles are practically of normal color.

Peritoneum is everywhere smooth and glistening. The mesenteric and omental fat is present in good amount, similar in shade to the subcutaneous fat. The general visceral arrangement is normal. Coils of small bowel are in general contracted, small, appendix region is free from adhesions. Bladder is distended with urine extending 11.5 centimeters above the symphysis. Diaphragm at the upper border of the 5th rib on the left, lower border of the 4th rib on the right.

Pericardium is smooth and glistening, contains 1 or 2 cubic centimeters of clear fluid. Heart is firmly contracted, measures 10.5 centimeters from the auriculo-ventricular ring to apex, surface smooth, sub-epicardial fat well-developed. The right side of the heart is practically empty, but for a small amount of fluid blood. Valves are normal and competent. The left side of the heart contains a small, dark, post-mortem clot. The mitral valves are normal as are the aortic. Base of the aorta is smooth and elastic. The wall of the left ventricle measures 2 centimeters at its thickest portion and the right measures 0.6 centimeter. The heart muscle is of a firm, reddish-brown color. Heart weight 300 grams.

Lungs: The left pleural cavity is obliterated, the lung being adherent to the chest wall and diaphragm by firm, old, fibrous adhesions. The lung is apparently crepitant everywhere, is pale and on section is air-containing throughout, of a pasty yellowish-gray color. The right lung lies free in its pleural cavity except at the base, where it is adherent to the diaphragm; it presents a similar appearance to the left. Apparently air-containing throughout. On section similar to opposite lung.

Spleen is small, measuring 7.3 by 4.5 by about 2.5 centimeters, surface smooth, color dark grayish-purple. On section there is a decided increase in the connective tissue. The pulp is moist, of a brownish color. Spleen weighs 35 grams.

Kidneys: The left kidney measures 10 by 6 by 4 centimeters, its capsule strips readily, leaving a smooth, pale yellowish surface somewhat mottled with areas of red. On section the cortex measures, 0.6 centimeter, entire organ is of a pale yellowish color, contains a very small amount of blood. The right kidney measures 9.8, by 5.5 by 3.5 centimeters, is similar throughout to opposite organ. Combined weight of the two organs is 270 grams. Suprarenals are normal.

Pancreas is firm, of a yellowish color. On section it is somewhat pale, although apparently normal.

Liver measures 24 by 14 by 8 centimeters, surface is smooth, edge sharp, organ is somewhat soft and putty-like. On section the parenchyma is of a brownish color, homogeneous. Gall-bladder contains several cubic centimeters of dark, slightly inspissated bile. Duct patent. Weight of liver is 1,020 grams.

Bladder measures 15 by 12 centimeters, walls are stretched and thinned. It contains a large amount of clear, amber-colored urine. Mucosa is very pale, otherwise normal. Prostate apparently normal.

Stomach: Mucous membrane extremely pale with small, hæmorrhagic areas near the pyloric end; otherwise the organ appears normal.

Small intestine: Contents, greenish mucus. The mucosa shows the same pale condition. Peyer's patches and solitary follicles prominent, but not congested. Numerous *Trichuris trichiura* are present, the greater number being found in the lower part of the ileum.

Large intestine: On opening the ileocæcal valve two hundred trichiuris are counted. These parasites extend the entire length of the gut. The mucosa of the descending colon shows a few healed amœbic ulcers. With the exception of the extremely pale condition of the mucosa, the organ appears normal.

Anatomic diagnosis.—Severe grade of secondary anæmia.

Specimens of the worms were submitted to Mr. G. F. Richmond, chief of the chemical laboratory, for determination as to the presence of pigments of blood origin and he reports that no such pigments are found.

Dr. Philip E. Garrison, medical zoölogist, Biological Laboratory, Bureau of Science, reports as follows:

"The whip-worms received on September 16 have been carefully examined and compared with specimens identified in Dr. Stiles' laboratory in Washington. They appear to agree in every material character with *Trichuris trichiura* (Linnaeus 1761) = *Trichocephalus dispar* Rudolphi, 1801. The specimens are No. 258 in the Bureau of Science Helminthological Collection."

CASE II.—*Severe infection with whip-worms, with diarrhœa, muscular cramps, dizziness, œdema and indigestion; patient left hospital after ten days observation.*

F. E., male Filipino, age 22, was admitted to St. Paul's Hospital March 10, 1906, and left March 21. His *family history* and the *history of previous diseases* give no data of importance. *Present illness:* For about six months previous to admission the patient has suffered from diarrhœa of a somewhat intermittent character. The stools were only one or two on some days, but generally they were from five to ten or more in twenty-four hours, being soft and pasty. Other symptoms during this time were dizziness, weakness, palpition of the heart, tinnitus aurium, cramps in muscles of the legs and chest, anorexia and indigestion.

On admission the patient complained of weakness, shortness of breath, palpitation of the heart, nausea, diarrhœa, ringing in the ears, partial loss of voice and melancholic tendencies.

Examination shows a pale, somewhat emaciated Filipino with moderate œdema of the feet and legs. Examination of the circulatory system demonstrates a weak pulse of 110 in the upright position: the arteries are soft and there is a soft murmur at the apex of the heart. The spleen not palpable, and blood examination is as follows: Erythrocytes, 2,400,000; leucocytes, 9,000; hæmoglobin 23 per cent.

There are no nucleated red cells and the differential leucocyte count shows a slight relative increase in large mononuclears. There is no eosinophilia. The respiratory system appears normal. Examination of the alimentary system gives the following details: Tongue, large and flabby with teeth marks on the edges, but no dark streak in the center. The abdominal examination is negative and the stool contains very many ova of *Trichuris trichiura.* The urinary system (including urine examination), the reproductive, cutaneous, and locomotor systems appear normal, except for moderate œdema of the lower extremeties. The reflexes are present and nothing abnormal is found upon examination of the nervous system.

During the patient's ten days' stay in the hospital, two unsuccessful attempts were made to remove the *Trichuris*. Both thymol in 6 gram and santonin and calomel in 0.250 gram doses were used. The patient left the hospital in a worse condition than when he entered.

In this case repeated and careful examinations were made and the data obtained could only be explained by assuming the cause of disease to be *Trichuris trichiura.*

CASE III.—*Trichocephaliasis with severe secondary anæmia; under observation and treatment for one month without improvement.*

D. V., a male Eurasian from Singapore came under our observation in September, 1904, and left the Philippine Islands in October of the same year. The family history and history of previous illnesses of this patient are unimportant.

Present illness.—About one year after arrival in the Philippine Islands the patient began to notice that he was becoming "anæmic," with shortness of breath and palpitation of the heart. About one month before he consulted us, diarrhœa developed and there was some œdema of the legs. At the time he came under our observation the principal subjective symptoms were dizziness, with shortness of breath and palpitation of the heart upon exertion, indifferent appetite, with nausea more marked in the morning, occasional vomiting, and moderate diarrhœa. There was a general feeling of "nervousness" and tendency toward melancholia.

Examination.—A rather severe secondary anæmia was present which could not be explained, except by the presence of a rather severe *Trichuris* infection. The stools after a saline cathartic often contained as many as 20 eggs in one field of the microscope, an AA objective and No. 4 ocular being used.

The blood examination was as follows: Erythrocytes, 2,800,000; leucocytes, 6,400; hæmoglobin, 36 per cent.

There were no nucleated red cells and the differential leucocyte count was approximately normal.

One unsuccessful attempt was made to dislodge the parasites by thymol. Good food, tonics, and general hygiene were prescribed, but the patient did not improve and he left the Philippine Islands about one month after we first saw him.

CASE IV.—*Embolism of the left coronary artery caused by an adult Trichuris trichiura.*[1]

It has not been possible to obtain a clinical history of very much importance in this case. The patient was a Filipino boy, 17 years old, and had been ill for about a week. For approximately the first five days he complained of pain in the chest, cough, shortness of breath, and he vomited once or twice. Slight diarrhœa developed and continued throughout the trouble. Pulse 130, temperature at first from 38° to 39°. Two days before death the symptoms became very much aggravated; vomiting more frequent, temperature 40°.5. Death occurred suddenly.

Autopsy (twenty-three hours after death).—Petechial hæmorrhages in skin of shoulders and occasional ones over the rest of the body. No glandular enlargements.

Lungs: Lower lobes much congested, dark, grayish-red in color. Center of outer surface of left lobe shows a hæmorrhagic infarct about 4 centimeters in diameter, penetrating about 3 centimeters into the lung substance. Lower edge of right lower lobe has a large infarct about 11 centimeters in length and about 6 centimeters broad. On section no embolism could be found in the arteries.

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[1] This case is not reported as one of importance in elucidating the question of the pathogenicity of whip-worms, but it is mentioned as being a very curious finding for which we have no explanation to offer.

Heart: Very slight atheromatous patches in arch of aorta. The left coronary artery contains an adult *Trichuris trichiura*, with about one-third of the posterior portion remaining free in the aorta.

Liver: The liver is friable, dark red in color (slight post-mortem change). The *spleen* is dark red, slightly mottled, and of firm consistency. *Kidneys* congested.

Moderate injection of the mucous membrane of the large intestine, which contains a small amount of mucus; a number of *Trichuris* were found in the cæcum.

Anatomic diagnosis: Embolism of the left coronary artery due to adult *Trichuris;* hæmorrhagic infarcts of the lower lobe of either lung.

Numerous other cases of *Trichuris* infection much less severe, but with suggestive symptoms, could be mentioned, but in them the diagnosis is not so clear and they will only be considered in the general discussion in the second part of this paper.

GENERAL REVIEW OF THE LITERATURE.

The first description of the parasite which we now recognize as *Trichuris trichiura* (Linnaeus 1761) was that of Morgagni (61) who found the worms in the cæcum of a man at autopsy. Röderer (73), in collaboration with his students, made additional contributions to the description of the parasite, and Büttner (1761) examining their specimens and mistaking the posterior for the anterior end of the parasite named it *Trichuris.* Linnæus (1771) introduced the name *Ascaris trichiura.* Goeze (34) recognized Büttner's error in thinking the smaller end to be the head of the parasite and changed the name from *Trichuris* to *Trichocephalos.* According to Blanchard (8) Morgagni, Röderer, Wagler, Happ, and Wristberg thought there were two species of these worms, but Müller (1778) showed the two kinds to be male and female; Schrank (1788) recognized the parasite under the name of *Trichocephalus hominis,* and the same name was used by Gmelin (1789); Rudolphi (1801) described the parasite under the name of *Trichocephalus dispar* and this name has been the one in most common use until within the last few years.

Owing to the adoption of different rules of nomenclature there is at present considerable difference of opinion among zoölogists as to the correct name of the parasite. Stiles maintains *Trichuris trichiura,* while most of the European authors adopt *Trichocephalus trichuris.*

Without entering into the discussion, we have decided in this report to use the name recommended by Stiles.

Barth (4) reports a case of severe infection with *Trichuris* as the only explanation of severe meningitis-like symptoms in a patient. This is perhaps the first report in which a pathogenic rôle in human beings has been attributed to this parasite.

Davaine (19) examined a large series of stools in Paris and concluded that probably one-half the people of that city harbor this parasite.

Gibson (32) reports an interesting case of severe nervous symptoms with paralysis in a girl who had a very severe *Trichuris* infection. Calomel 0.065 gram and rhubarb powder 0.65 gram were given night and morning for some days. "On two occasions the child passed a small chamber vesselful of worms; species, *Trichocephalus dispar.*" More worms were passed on another date and following this, the child rapidly recovered.

Pascal (67) reports the case of a girl, 4 years old, who died of brain symptoms simulating meningitis. Many *Trichuris* were found in the intestine at autopsy and no pathologic changes were discovered. The author believed the parasites to have been the cause of death.

Burchardt (14) reports two cases in which he regarded *Trichocephalus* as the causative agent. Vomiting, diarrhœa, headache, dizziness, and marked anæmia were present in his first case. There was slight improvement upon treatment, followed by relapse with icterus, bloody vomit, aphonia, and marked anæmia. Complete recovery followed the expulsion of a large number of the worms. Burchardt's second case was similar to the first, excepting that the symptoms including the nervous ones were much less marked.

Mégnin (56) pointed out the fact that dogs which harbor large numbers of a *Trichuris* suffer from a pernicious anæmia.

Lutz (53) working in Brazil, found eggs in the stools of man, pigs, and cats. In man, about one-third of the specimens examined contained the ova.

Erni (24) believed the Trichuris to be one of the causes of beri-beri.

Grassi (35) describes the swallowing of *Trichuris* eggs by a student who 28 days later found the first eggs in his stools.

R. Blanchard (9) in a review of the subject of *Trichuris* infections states that Vix, Leukart, and Brumpt all give observation of the transfixation of the mucosa of the caecum by *Trichuris* and believes that this definite fastening of the worms explains their constant absence from the fæces in infected cases. However, Klebs (50), Heller (45) and Wichmann (89) do not believe that the worms attach themselves to the mucosa, but state that they are maintained in place by a mucus capsule resting upon the mucous membrane.

Moosbrugger (59) reports three cases. The first was in a boy a year and a half old who had a severe diarrhœa and with the usual symptoms accompanying the latter. During an attack of bronchitis with fever the eggs of *Trichuris*, which had been very numerous in the stools, disappeared. The author's second case was in a three year old boy with symptoms similar to those in the first. The patient died of croup and at the autopsy 442 male and 445 female worms were removed from the bowel. The mucous membrane was pale in some places and in others there were zones of congestion, with red spots and some erosions and ulcerations in others. The third case was that of a girl three and half years old, who had suffered for six months with severe diarrhœa of twenty or more stools daily. The stools were tough in consistency and usually contained some blood. There were 1,650 *Trichuris* eggs in one cubic centimeter of fluid stool. The child was very anæmic, but recovered under treatment. Moosbrugger considers the parasites to be the cause of the symptoms in his cases.

Boas (11) considered the *Trichuris* to be the cause of severe chronic diarrhœa, emaciation and anæmia in his patient, who was a man 71 years old.

Huber (47) considers the clinical significance of this parasite to be generally underestimated. He notes the presence of the worms in the cæcum, appendix, and occasionally in the ileum. The symptoms depend upon the severity of the infection and are local (diarrhœa) and reflex (aphasia, etc.).

Askanazy (3) demonstrated an iron-containing pigment in the intestinal epithelial cells of *Trichuris* and concluded it to be a blood-sucking parasite. He also showed that the parasite attached itself to the intestinal wall by piercing a loop of mucosa or by inserting the head into the glandular tubules of the mucosa. He believed that during certain diseases, or after death of the host, the parasites disengage themselved from the mucous membrane and that this fact explains why at autopsy they are usually found free in the intestine. Becker (5) in accepting the hypothesis of Askanazy, explains his failure to secure the worms when his patient was treated with benzine, by stating that the worms were killed in place and so remained attached to the mucosa.

Morsasca(62) reports one case of severe progressive anæmia accompanied by abdominal pains, nervous symptoms, and diarrhœa and considers that *Trichuris*, which were present, to be the cause of the condition.

Federolf(27), a Russian military surgeon, notes that Russian authors have repeatedly called attention to the serious symptoms which may be produced by *Trichuris* infections. He reports one case in which the prominent symptoms were psychic depression, slight diarrhœa, retention of urine, fever of intermittent character, nausea, and palpitation of the heart. Treatment by santonin was followed by the disappearance of the eggs from the stools and the complete recovery of the patient.

Heine(43) encountered *Trichuris* in many sick deer and in two of the animals which he found dead the presence of these parasites was the only condition which could explain the result. Hausmann(42) believes that certain of the symptoms of infection with this parasite point to the production of some form of toxin. Guinard(41) reports finding nematode worms in the cæcum at operations for appendicitis.

Metchnikoff(57) considers both the clinical and pathologic facts to be convincing of the important rôle of eelworms and whip-worms in appendicitis. Guiart(39, 40) insists upon the important pathogenic rôle of *Trichuris* in human pathology. The parasite fixes itself on the mucous membrane of the cæcum or appendix and becomes an inoculating agent of bacteria. In one case of appendectomy an adult *Trichuris* was found attached to the mucosa of the appendix and the author believes it to have been the cause of the disease.

Girard(33) reports a case of appendicitis with general peritonitis due to infection with *Trichuris* (*Trichocephalus hominis*). The patient was a girl, 8 years old, who was recently convalescent from typhoid fever. She was re-admitted to the hospital suffering from diphtheria and a vaginal discharge. Under antitoxin treatment there was recovery from the diphtheria. Symptoms of acute, severe appendicitis developed and the appendix was resected on the fourth day. At operation a general peritonitis was encountered and after resection of the appendix and drainage, complete recovery resulted. The appendix was fixed *en masse* and sectioned. In general the organ showed but slight pathologic change except in the distal third where there was rather severe inflammation. Section in this area showed partial occlusion of the lumen caused by two of the adult *Trichuris* which were firmly attached to the mucosa. The author describes and illustrates the inflammatory zone around the attachment of the worms to the mucosa and, although no perforation is mentioned, he considers the peritonitis to be due to the condition of the appendix. Finally, Girard believes he has demonstrated the penetrating powers of the whip-worm; he states that the parasites play a septic rôle at least by transmission of pathogenic bacteria and he believes with Metchnikoff, that these parasites may cause inflammatory lesions which may lead to grave consequences.

Schiller(75) reports a case of heavy infection with *Trichuris* in which high fever was a symptom. Hemmeter (46) considers that single specimens of the parasite do not cause symptoms, but if larger numbers occur in the colon, diarrhœa and nervous symptoms may appear.

Becker(5) reports two cases of *Trichuris* infection. In the first the patient was a woman suffering from chronic progressive anæmia with dizziness, cramps in the muscles, abdominal pain, and palpitation of the heart and the stools contained many *Trichuris* eggs. Physical examination was negative. At the time she came under the author's observation the blood examination showed as follows: Marked poikilocytosis and macrocytes were numerous; erythrocytes 3,456,000; leucocytes 6,250; hæmoglobin 35 per cent. After three week's observation it was: Erythrocytes 3,200,000, leucocytes 6,000, hæmoglobin 25 per cent. The differential count of the leucocytes showed: Polymorphonuclears 69, lymphocytes 26, mononuclears 3, eosinophiles 2. There were no nucleated red cells. Numerous *Trichuris* eggs were present in the stools. The patient was treated with eight enemas of solutions of benzin. No parasites were found during or after these treatments, but the eggs disappeared from the stools and were not again seen. The patient rapidly recovered after the disappearance of the eggs from the stools. The author's second case was that of a woman 26 years old suffering from chronic progressive anæmia, palpitation of the heart, dizziness, nausea, and diarrhœa. The stool contained numerous *Trichuris* eggs. The physical examination was negative. The blood examination showed: Erythrocytes, 2,852,000; leucocytes, 8,700; hæmoglobin, 25 per cent. Normoblasts were numerous but megoloblasts were not present. There was some improvement in this case under treatment by arsenic and iron. The patient left the hospital before further observation could be made. Becker believes the *Trichuris* to be responsible for the condition in both these cases and furthermore compares its action with that of *Agchylostoma* and the *Dibothriocephalus latus.*

Ward(88) states that since Askanazy has shown the occurrence of hæmoglobin in the alimentary canal of these worms, the fact that they nourish themselves on the blood of the host can not be doubted.

Sandler(74) reports a fatal case in a boy twelve years old. The patient when admitted to the service complained of fainting spells, anæmia, weakness, palpitation of the heart, fever of an irregular, intermittent type, yellow and brownish spots on the legs, headache, nausea, vomiting, diarrhœa with blood at times, abdominal pains and tinnitus aurium. On examination there was marked anæmia, hæmic murmur of the heart, and weak, rapid pulse. The spleen and lymphatics were not enlarged. Blood examination showed: Erythrocytes, 1,200,000; leucocytes, 30,600; hæmoglobin, 28 per cent. There was poikilocytosis, but no nucleated red cells. The stools contained eggs of *Trichuris.* After about two weeks of treatment and observation the blood examination was as follows: Erythrocytes, 690,000; leucocytes, 14,000; hæmoglobin, 20 per cent. The patient's condition grew progressively worse with accentuation of the principal symptoms mentioned, and others also developed. There was bleeding of the nose, the sense of fear became marked, fever became more severe, reaching 39° in the afternoons, and for some time before death which occurred in coma, there was delirium and very frequent vomiting. The diarrhœa improved so that the bowels were practically normal for some time before death. Autopsy could not be obtained, but the author is convinced that *Trichuris* was the etiologic factor in the condition.

French and Boycott(28) in reporting upon the prevalence of *Trichuris* infections in the patients in Guy's Hospital, London, makes the following observations. Stools of 500 patients were examined and *Trichuris* eggs were found 39 times or 7.8 per cent. The infection was rare in children under 5 years of age and was about equal in the sexes. The authors also compile the statistics as to prevalence from the following sources: Leuckart(52) in Erlangen 11.1 per cent, Erlangen insane 100 per cent, Dresden, 2.5 per cent, Kiel 32.2 per cent; Cobbold(17) in Dublin 90 per cent, Greenwich 69 per cent; Davaine(20) in Paris 50 per cent, Naples 100 per cent; Blanchard(9) in Bâle 23.6 per cent; Garrison, Ransom, and Stevenson(31) in 10.8 per cent of insane; Ashford, King, and Igaravidez(2) 6 per cent; Boycott(12) in Cornish Miners 79 per cent. Garrison(30) working in the Philippine Islands found the infection in 59 per cent of adult prisoners.

Osler (65) states that "The *Trichocephalus* rarely causes symptoms." He notes without comment the recent observations in which severe anæmia has occurred in connection with infections with this parasite. Allen J. Smith (80) considers the parasite to be of little pathologic importance, stating that apparently it does but little damage and practically never gives rise to appreciable symptoms of its presence. Emerson (23) states that "This parasite is harmless as a rule, but may cause enteritis and the severest and even fatal anæmia."

Poledne (68, 69) reports one case. The patient was a sailor who was admitted to the hospital suffering from fever and severe diarrhœa. The fever was typhoid in character, but careful examination by modern laboratory methods gave negative results for typhoid, paratyphoid, Malta fever, and tuberculosis. Anæmia, emaciation, and nervous symptoms were present. The blood showed a slight leucocytosis and a relative eosinophilia. There were numerous ova of *Trichuris trichiura* in the stools. The fever and diarrhœa subsided after treatment by thymol and by benzine enemas, the eggs disappeared from the stools and a rapid and permanent cure followed.

Vix (86) considers the parasite to be pathogenic and states that it may produce ulceration of the intestinal mucosa. Rippe (72) reviews the literature of *Trichuris* infections and reports two cases occurring in Russia. His first patient was a woman who had been ill for three years. The important symptoms were nausea and vomiting, anorexia, weakness, dizziness, muscular pains particularly in the legs, slight diarrhœa, and melancholia. On examination there was emaciation, marked pallor of the mucous membrane and some abdominal distension with tenderness over the cæcum. The stools contained mucus and numerous eggs of *Trichuris*. After treatment by thymol the eggs disappeared from the stools and the patient made a rapid and permanent recovery. The second case was in a man who was suffering from a purulent pleuritis, with frequent epileptoid seizures, diarrhœa, muscular cramps, nausea, and restlessness. There were numerous eggs of *Trichuris* in the stools. The patient died and at autopsy the brain was normal, except for slight œdema of the meninges; the mucous membrane of the cæcum and lower portion of the small intestine was hyperaemic and contained *Trichuris trichiura*. Rippe considers *Trichuris* to be a pathogenic parasite and that infection with it must be considered in making diagnoses in conditions showing intestinal and nervous symptoms. The author found the eggs in 42.93 per cent of 184 cases of parasitic infection of the intestine in Russia.

Stiles (82) treats the pathogenicity of this parasite in a conservative manner. He recognizes a lack of symptoms in the majority of light infections, but on the other hand this author makes the statement "that severe infections do not produce injury is not in accordance either with probability or with recorded observations." Again he states that "several cases of severe anæmia have been recorded within recent years which were, apparently justly, attributed to heavy infections with whip-worms." Kahane (48) considers the parasite to be pathogenic. He states that it can cause ulceration of the intestinal mucosa and that the head may penetrate the walls of the bowel to the muscular coat.

Sir Patrick Manson (54) considers *Trichuris* infestation of no practical moment and that, so far as known, the parasites give rise to no serious pathologic lesions. Manson and Shipley (55) state that so far as is known *Trichuris* has very little pathologic significance, except when it perforates the intestine. These authors call attention to reports in which nervous symptoms have been associated with a high degree of infection. According to the same authors "several cases of anæmia (some fatal) are reported as caused by the presence of this parasite, the blood showing a fall in the number of red cells, marked poikilocytosis, and the appearance of nucleated red cells principally of the normoblastic type." Eosinophilia has been noted, but is not the rule.

Braun(13) considers *Trichuris* to be pathogenic. Seifert(78) states that from the evidence of recent years it is necessary to remove *Trichuris* from the list of commensal parasites and place it among those pathogenic for man, and that the prognosis is grave in some severe infections.

TRICHOCEPHALIASIS.

SYNONYMS.—Whip-worm infection, Trichuriasis.

DEFINITION.—An infection with whip-worms, usually confined to the large intestine, less frequently to the appendix and ileum and occasionally by perforation invading other parts of the body. In light infections there are no pathologic changes or symptoms of importance, but the heavier infections are characterized by anæmia, which may be very severe and even fatal and by nervous and gastrointestinal symptoms.

ETIOLOGY.—Contributing causes: The ordinary causes which usually are considered as influencing infections probably play a less important rôle here than with many other diseases.

The geographic distribution of the infection is cosmopolitan. It is particularly prevalent in the Philippine Islands.

Sex.—Practically all authors recognize the much more frequent infection in females. Stiles and Garrison(83) in 3,457 cases found 12.13 per cent of infections in females and 10.08 in males.

Age.—It is generally recognized that infections are most prevalent during childhood and gradually grow less with advancing age.

Garrison, Ransom, and Stevenson(31) in 500 examinations noted this gradual decrease of infection with age, and Stiles and Garrison(83) found the following percentages of infection according to age: Under 15 years 13.01; from 15 to 30 years 10.09; from 31 to 50 years 8.65 and over 50 years 4.65. Garrison's(30) statistics in the Philippines were based entirely upon examination of specimens from adults and in our service the number of recorded examinations for children is too small to make statistics of value. However, we have seen several instances of infections in breast-fed infants, in one case the child being less than 3 months old.

Race and nationality.—In general it may be stated that the infection is more frequent among the colored races than it is in the Caucasian. Stiles and Garrison noted particularly the preponderance of infections in the American negro over that of the white races of the same country. Our records show a much higher percentage of infection in native Filipinos than is found in the foreign residents of the Caucasian race resident in Manila. In Stiles and Garrison's statistics, Irish born patients showed a higher percentage of infection than did any other nationality resident in the United States.

Residence.—The infection is more common in rural districts than it is in cities, no doubt largely because of the better methods of disposal of fæces in cities.

Occupation.—The infection is more frequent among soldiers, laborers and others whose manner of life and occupation brings them into contact with faecal infected substances.

Overcrowding with its usual insanitary surroundings may readily be inferred to be a factor in incidence.

Climate.—It is generally stated that the infection is more frequent in warm climates.

Gastrointestinal condition.—There are no statistics available, but it is probable that it is not a factor in the incidence of this infection.

Environment and mode of life.—After all is said regarding the influence of race, sex, etc., upon the prevalence of this infection, it is probable that the question of infection or noninfection is almost entirely due to the mode of life of any given individual or community. In other words, it is a question of exposure, which in the vast majority of instances occurs only in those who are ignorant, or whose personal hygiene is otherwise very faulty. ***In a sense, it seems to us, that the prevalence of whip-worm infections in a community is, to a certain extent at least, an index of the intelligence and cleanliness of its citizens.*** This statement makes the assumption of what is probably a fact, that physiologic predisposition to infection with this parasite (except perhaps in children), if it exists at all, surely does so to a very minor degree.

Stiles and Garrison in discussing the question of physiologic predisposition in females state that "the relative frequency of a given parasite, or of helminthiasis in general, among males and females is apparently not so much a question of physiologic predisposition of the sex toward the parasite, as it is a question of the relative intimacy existing between the average daily life of the sex and the more concentrated infectious material."

In the case of whip-worm infections it seems to us that this statement applies not only to a question of sex, but that it explains many of the differences noticed under predisposing causes. Carrying this statement to its logical conclusion, we may say that race, sex, occupation, etc., as such, probably are not factors in the incidence of the infection, except to the extent in which they harmonize with the person's exposure to sources of infection under a given mode of life.

TRICHURIS.[2]

This *genus* is easily recognized by its peculiar whip-worm shape; the thick posterior portion and the long, slender anterior portion representing the stock and the lash respectively. The anterior extremity bears a small, round, mouth opening, behind which lies a small, funnel-shaped oral cavity. The long, thread-like œsophagus extends throughout the greater portion of the anterior, slender part of the body and enters the intestine which, in a folded course, reaches the posterior extremity of the body to find exit at a terminal anus in the female, and at the common genito-anal orifice in the male. The cuticle is striated transversely, except on the ventral surface where a longitudinal band, set with minute papillæ, extends from the anterior to the posterior extremities. The thick posterior portion of the body contains the intestine and the genital organs. In the female it is straight or slightly bow-shaped; in the male it is more or less closely coiled.

Male organs.—The testicle is single and consists of a long, coiled and folded tube which fills the greater part of the caudal portion of the body. A short, broad *vas deferens* turning abruptly caudad from the anterior end of the testicle enters a dilated portion of the genital tube (*vesicula seminalis*) which, in turn extends posteriorly to the cirrus or spicule. The spicule is single, highly developed and lies in a sheath or cirrus pouch, both sheath and spicule being protrusible for a considerable distance through the cloacal orifice.

Female organs.—The ovary is simple, tubular, with its extremity attenuated into a slender oviduct which enters the posterior end of the more expanded uterus. From the anterior extremity of the uterus, the slender, more or less coiled vagina leads to the genital pore which is situated on the ventral surface at about the junction of the slender, anterior and the thick, posterior portions of the body.

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[2] These diagnoses of this genus and species, furnished by Dr. Philip E. Garrison of this laboratory, are taken from various authors, chiefly Leuckart, with the purpose of furnishing for medical men a description of the parasite, not too technical, but rather more detailed than that usually given in medical publications.

The ova are barrel-shaped and are characterized, as are those of *Trichosoma*, by the little colorless plug which closes each end of the brownish shell.

Habitat.—The cæcum and, less frequently, the colon and ileum of certain mammals.

Several species of *Trichuris* are recognized for different hosts, namely, *Trichuris trichiura* of man and apes; *T. affinis* of sheep, goats, and cattle; *T. depressinsculus* of the dog and fox; *T. unginculatus* of the rabbit; *T. crenatus* of the pig. These species are distinguished morphologically chiefly by the size and structure of the spicule and its sheath.

Trichuris trichiura (Linnæus, 1761).

Male, 40 to 45 millimeters long; spicule, 2.5 millimeters long; sheath covered with small, evenly distributed papillæ. Female 40 to 50 millimeters long, length of slender anterior portion to length of thick posterior portion as 3 to 2. Mouth opening simple and with appendages. Ova yellow to brown, 50 to 54 millimeters long by 23 millimeters broad; unsegmented in fresh fæces.

Habitat.—Cæcum and, less frequently, colon and ileum of man, apes, and the lemur.

Development.—Simple, without intermediate host. Embryo develops in water or moist earth in from 3 to 6 months or longer and will remain alive in its shell for several years unless ingested by its final host when it hatches and reaches sexual maturity in the cæcum after about 16 days.

The resistance to the action of physical and chemical agents shown by both the parent and eggs is remarkable. The parasite is the most difficult of any to destroy in the intestine. The ordinary anthelmintics as a rule have little or no effect upon it. The eggs may be frozen or completely dried without doing them permanent injury.

MODES OF TRANSMISSION.—*Direct:* Inasmuch as an intermediate host is not necessary for the propagation of this parasite, and inasmuch as contact with fæcal discharges is necessary in order to receive the eggs into the gastro-intestinal canal, infection proves a closer personal contact with filth than is true of many other parasitic infections. However, because of the slow development of the eggs under outside influences, immediate transmission from person to person or auto-reinfection can not occur.

Water when contaminated with fæcal discharges, directly or indirectly, may become a transmitter of infection, but because of the rapidity with which the eggs are sedimented in water, it would seem as if this were a much less important medium of transmission than it is generally considered to be.

Food, particularly uncooked vegetables, and to a less extent, fruits, are undoubtedly a means of transmission in a considerable number of instances. On two occasions during our study of the washing from fresh vegetables for the presence of amœbæ, ova of *Trichuris* were found in the sedimented material. The danger from fresh vegetables is great in those countries where human fæces are used as fertilizer for the vegetable gardens. Although this procedure is a violation of the law, it is certainly practiced to a considerable extent by Chinese gardeners in the Philippines, as it is in several other oriental countries.

Insects, such as flies, water bugs, roaches, etc., may be factors of some importance as transmitters of the infection by mechanically carrying it from infected fæces to food and water supplies.

Soil, in localities where methods of sewage disposal are primitive, surely becomes infected and because of the great viability of the eggs in earth, such places become a menace in many obvious ways. So-called clay eaters would be especially liable to infection.

Air, clothing, dust and other substances may be considered as possible factors in the spread of the infection in a mechanical way.

Animals.—Several authors have called attention to the possible inflence of animals in the transmission of this infection. When it is remembered that some domestic animals used as pets may harbor this parasite, and that from their habits several of them are likely to have the eggs in their hair, it would seem that animals might be expected to be occasional transmitters of the infection, particularly among children.

PATHOGENICITY.—The largely accepted commensalism of this parasite is not in accord with the majority of the carefully reported observations (see literature review), nor is it borne out by study of our cases. Belief in the harmless character of *Trichuris* is based largely upon two observations: first, the great, general prevalence of the parasite without symptoms, and second, no satisfactory explanation of the nature of its pathogenic action has been offered.

If we examine the first of these in comparison with some other parasitic infections we find it to be a difference in *degree only* and not a peculiar condition. For example, *Uncinaria* are accepted as pathogenic parasites and yet in our service more than 90 per cent of individuals harboring the worm show no symptoms whatever of the infection. The first symptoms of infection with amœbæ may be those of peritonitis from a perforating ulcer.

Strongyloides stercoralis is now generally accepted as a pathogenic parasite, and yet in the vast majority of instances no symptoms are produced by its presence, and similar statements may be made regarding *Balantidium coli, Dibothriocephalus latus* and a number of other parasites usually accepted as pathogenic.

The percentage of cases infected with *Trichuris* without symptoms probably is greater than for any of the above-named parasites, but infections do occur which produce symptoms and the degree of difference does not appear to be great enough to justify it as an argument for the commensalism of *Trichuris.*

As to the second of the two views, that no satisfactory explanation of the nature of the infection has been made, we may at least in part answer that here the difference from some of the other parasites is also one of degree. No satisfactory explanation of the exact manner of the production or character of the lesions, produced by the majority of the intestinal parasites of man, has been offered.

The pathogenic character of *Trichuris* has been explained by considering it to be a blood sucker; by believing it to produce a hæmolytic substance such as is also acredited to hook-worms; by the formation by it of a toxin; by mechanical action and by its producing perforations which open a way for the entrance of bacteria. None of these explanations is supported by sufficient data to justify its acceptance. The majority of the repeated statements that the parasite is a blood sucker are credited to Askanazy. What Askanazy actually said was that he had isolated "an iron containing pigment from the epithelial cells of the intestine of the parasite." So far as we know, neither blood nor other positive evidence of blood absorption has been found in *Trichuris*.

These parasites do attach themselves to the intestinal wall during the life of the host by transfixation and direct penetration by the head end, and that these locations may show bright, hyperæmic spots and become eroded or even ulcerated, is proved beyond doubt. However, the lesions formed by this action are not as a rule sufficient to explain the symptoms, unless we accept some peculiar hæmolytic or other toxic action of the parasite. It is certain that the mechanical loss of blood from these infections is not sufficient to account for the symptoms and a definite toxic action has not been proved. The nervous symptoms and some of the gastro-intestinal ones might be explained from the mechanical action of the parasites by an hypothesis similar to that of Mayo's embryologic formation used for the explanation of similar symptoms in certain cases of chronic appendicitis and gall bladder diseases. However, this is only a hypothesis and does not account for the severe anæmia, which after all is the important manifestation. The nature of the action of these parasites in producing disease has not been satisfactorily explained, but this should not be accepted as proof of their commensalism.

PATHOLOGY.—The general pathologic changes in fatal cases of trichocephaliasis are severe, secondary anæmia. The special conditions are the presence of the worms and certain changes at their points of attachment to the mucous membrane of the bowel or appendix. Several changes have been described by different authors, which in the main are hyperæmia of the mucosa with hæmorrhagic points; erosions and superficial ulceration of the mucous membrane, surrounded by areas of cell infiltration; and in some instances deep ulceration or other inflammatory reactions extending to the muscular coat of the bowel. Several observers have shown that the worms are attached to the mucous membrane during the life of the patient. They attach themselves by transfixing a fold of mucous membrane, by penetrating the glandular follicles, and by direct perforation, the head being embedded in the deeper layers of the bowel wall. After the death of the patient, the worms detach themselves and at autopsy are usually found free in the bowel. Several authors have demonstrated this direct attachment to the intestine. Corroborative evidence is furnished by the fact that they do not appear in the discharges even after violent purgation. The worms were not passed in a number of cases of successful treatment, when the disappearance of eggs from the fæces showed that they had been destroyed. In these instances we can only assume that the parasites have been killed and remain attached to the mucous membrane of the intestine after death.

INCIDENCE.—This is one of the most frequent of all parasitic infections of man and Garrison has shown it to be the most prevalent in the Philippine Islands.

Some of the statistics in percentages are as follows:

French & Boycott (1905), London 7.8; (1887), Erlangen, 11.1; (1887), Erlangen (Insane), 100. Leukart (1887), Dresden, 2.5; (1887), Kiel, 32.2; (1879), Dublin, 90. Cobbold (1879), Greenwich, 69; (1877), Paris, 50. Davaine (1877), Naples, 100. Blanchard (1889), Bale, 23.6. Garrison, Ranson, and Stevenson

(1903), United States (Insane), 16.8. Heisig (1893), Germany, 45.21. Gubareff (1896), Russia, 43. Boycott (1904), England (Cornwall), 38.78. Grechaninoff (1890), St. Petersburg, 26.41. Sievers (1887), Kiel, 19.81. Roth (1877–1880), Bale, 26.67. Gribbohm (1872–1877), Kiel, 32.20. Heller (1872–1875), Kiel, 30.60. Müller (1862–1873), Erlangen, 11.11. Müller (1852–1862), Dresden, 2.57. Stiles and Garrison (1906), United States (Insane), 7.72. Cima (1893 and 1896), Italy, 37.27. Anæmia Commission (1904), Porto Rico, 7.27. Daniels (1901), Africa, 2.79. Fearnside (1900), India, 6.95. Dobson (1893), India, 4.40. Garrison (1908), Philippine Islands, 59.

Some of the figures included in the series are from examinations of only a few cases or were compiled under conditions which prevented the findings being properly considered as an index of the prevalence of the infection in the general population of the community in which the examinations were made.

Garrison's large and carefully worked out statistics show the highest percentage of infection among the general population as yet reported for any country.

The *incubation* period in this disease would be the time for development of the ingested embryo to maturity which, to judge from the few available data, is more than four weeks.

SYMPTOMS.—We recognize for convenience in discussion *mild* and *severe* intestinal trichocephaliasis and trichocephaliasis of the *appendix*. In general the symptoms may be said to depend upon the severity and location of the infection. In *mild* cases of intestinal infection there are no noticeable symptoms and the patient may harbor the parasites in considerable numbers for a long time without inconvenience. In *severe* infections the symptom complex is largely that of a severe secondary anæmia, with pronounced nervous symptoms and some gastro-intestinal disturbance. The early symptoms vary somewhat in different cases. Usually there is weakness, shortness of breath, nausea, vomiting, diarrhœa, cramps in the muscles, nervousness, insomnia, and a gradually developing anæmia. The condition is as a rule progressive, with accentuation of the principal symptoms as the disease advances.

Circulatory system.—Weakness, with shortness of breath and palpitation of the heart are often early symptoms and become more marked as the disease progresses. Evidences of anæmia, such as pallor of the mucous membrane, œdema, and hæmic murmur of the heart have been noted in several cases. As a rule the spleen is not enlarged and in fact, it may be smaller than normal. The blood picture is largely that of secondary anæmia. There is a decrease in the number of red cells, with poikilocytosis, but nucleated cells are not as a rule present. The number of the leucocytes remains approximately normal and the differential count usually shows a slight relative increase in mononuclears. Slight eosinophilia has been noted, but most observers agree that the eosin cells are not increased and in our cases eosinophilia was absent. No eosin cells were ever found in our Case No. 1. The hæmoglobin is reduced and may be very low before death.

The symptoms in the *respiratory system* may consist of some dyspnœa and cough, when severe anæmia is present.

The *alimentary system* as a rule suffers rather severely. Nausea and vomiting are frequent and annoying symptoms, anorexia and dyspeptic symptoms are also often encountered, although the appetite may remain good throughout the course of the disease. The mucous membranes are pale, the tongue often large and flabby and in two of our cases it showed a dark band down the center, similar to that which has been described for uncinariasis. There may, or may not, be tenderness and pain in the gastric region and in the two cases where it has been recorded, examination of the stomach contents showed nothing abnormal. More or less abdominal discomfort or even pain has been a feature of the majority of cases which have been described and diarrhœa has been present in most of them. The character and number of the intestinal discharges varies, ranging from only one or two stiff, pasty stools in twenty-four hours, to the severest form of diarrhœa, even with bloody discharges. Again, the bowel movements may appear normal for considerable periods of time. Whatever the number and character of the bowel movements, tenesmus and other symptoms indicating involvement of the lower bowel are rare. Stool examinations demonstrate the eggs of the *Trichuris;* at times but few, and again large numbers may be seen in a single field of the microscope. The *urinary, reproductive,* and *locomotor systems* do not, as a rule, show any characteristic symptoms. Muscular cramps, particularly in the calves of the legs, have been repeatedly observed. The urine is usually normal. The *cutaneous system* shows the changes due to anæmia. There may be more or less œdema of dependent parts and even anasarca may develop. The superficial lymphatics are not enlarged.

The *nervous* symptoms are usually quite noticeable and consist of mental and nervous depression which may be melancholic in character; there is often great restlessness, headache, and sometimes insomnia. Objectively nothing of importance is found.

Among the symptoms of the *special senses* aphasia is frequent and it is difficult to explain. Tinnitus aurium and even partial deafness have also been noted by several observers.

Appendiceal trichocephaliasis has not heretofore received much attention. Metchinkoff urged its importance and reported a convincing case in detail. Very little is given about the clinical findings, but *a priori* there is no reason to assume that they would be materially different from appendicitis of other etiology.

Trichocephaliasis of animals has been observed by several authors.

Analysis of symptoms.—As pointed out by Becker, the symptoms in the majority of cases of this disease fall into three groups:

(1) Those of the blood, (2) nervous and (3) gastro-intestinal symptoms.

These are present to a greater or less extent in all cases of severe infection. The blood changes and the anæmia point positively to what we recognize as a secondary type of the latter. The absence of eosinophilia is quite generally recognized and is to be noted. French and Boycott paid particular attention to this condition and failed to find eosinophilia in 26 cases which they examined. In ours, eosinophilipænia was the rule, and in Case No. 1 no eosinophile cells were ever found after repeated blood examinations.

The nervous symptoms are difficult to explain, particularly the mental and nervous depression and the aphasia which has been so frequently noted, and it is probable that the nausea and vomiting are to a considerable extent of nervous origin.

Even the intestinal symptoms are difficult to explain as a result of the pathologic findings, certainly they are not to be considered as being due to the direct loss of blood caused by the mechanical action of the worms. Marsasca and others believe that the latter secrete a special toxin, and although the entire clinical picture supports such a view, it has not been demonstrated. Bacteria and other secondary invaders entering through the injured mucosa probably account for some of the symptoms and explain those cases having septicæmia. However, the manner of the production of the symptoms remains unexplained.

DIAGNOSIS.—While the clinical picture in some of these cases is quite suggestive, diagnosis can only be determined by finding the eggs of the parasite in the stools. Not every patient having eggs in the stools will show symptoms of the infection, and for clinical purposes only a combination of some of the clinical phenomena and the presence of eggs should be considered as a diagnosis from a practical therapeutic standpoint. The differentiation from most of the other recognized types of anæmia is readily made by the blood picture. Severe infections are only differentiated clinically from similar cases of uncinariasis by stool examinations and by the greater prevalence of eosinophilia in the hook-worm infections.

PROGNOSIS.—Certain light infections do not appear to do recognizable harm, even when the parasites remain for a long time in the bowel. The prognosis in severe infections is grave, largely because of the difficulty with which the parasites are destroyed. Barth, Pascal, Sandler, Moosbrugger and others have reported fatal cases. The disease may continue for a long time, and, on the other hand, as in our Case No. 1, the course may be fairly acute and its duration from the development of clinical symptoms short.

PROPHYLAXIS.—The prevention of this disease consists in personal hygiene and in public health measures. Because of the simple life cycle of the parasite and the long viability of the eggs under outside influences, personal hygiene, by avoiding the introduction of unsterilized substances into the mouth, makes protection fairly safe even in infected zones.

The hygienic side of the problem requires a safe and practical method for the disposal of fæces. This is very important, not only because of the presence of whip-worms, but of others as well. This subject has been covered by Garrison (30).

TREATMENT.—Whip-worms are exceedingly difficult to destroy in the intestine. In this respect out experiences have been in conformity with the general literature of the subject. However, several authors have had more or less success with various anthelmintics, *and in most cases where it has been possible to destroy the worms, rapid and complete recovery of the patient has followed.* Enemas of solutions of benzine have been the most successful in the hands of several observers, while others have reported success by the use of calomel, thymol, naphthol, santonin, or garlic. We have used thymol, the eucaliptus oil, chloroform, and the castor oil mixtures employed for uncinariasis, but without very much success. The benzine treatment has only just come to our notice, but to judge from the reports in the literature it deserves a more extended trial. Schiller (quoted by Sandler (74)) used thymol by mouth and benzine solutions as enemas and secured 2,000 worms from one case. This is remarkable because of the fact that the worms were passed. The killed worms in the experience of most authors do not pass from the bowel and their destruction is only made evident by the disappearance of the eggs from the stools. Other treatment of the disease consists in general hygienic measures with attempts to improve the nutrition of the patient.

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EDITORIAL.

NEOPLASMS AMONG THE FILIPINOS.

It has been variously stated by different writers that new growths and more especially malignant tumors, are not only less common than in temperate climates, but even rare in many tropical countries. There was a more or less well-defined idea prevalent among the profession in Manila that in the native inhabitants of the Philippines neoplasms are uncommon, but no complete records were available bearing on the point.

Malignant disease as a cause of death occurred twice among the first series of 100 necropsies at the Philippine Medical School; 2 cases of carcinoma of the greater curvature of the stomach, and 1 of the cheek and antrum.

Dudley,[1] writing on the prevalence of cancer in the Philippines after an experience of ten years spent in the various islands, believes that cancer exists in the Philippines to a greater extent than in the United States, and that the statistics available on malignant and nonmalignant growths are very incomplete.

The following figures illustrating the frequency of neoplasms in Dr. McDill's surgical clinic at the St. Paul's Hospital may be taken as fairly typical, as the clinic draws on all classes of free patients, the material coming not only from the city of Manila, but from the surrounding and often distant provinces.

The record of cases coming to operation from September 5, 1907, up to December 19, 1908, shows a total of 377. Sixty-five of these cases, or 17.4 per cent, were operations for new growths, 37 benign and 28 malignant.

Of the benign neoplasms, cystic ovarian disease leads in frequency, there being 16 cases, of which 4 were double. Of uterine fibroids there were 7 cases, the most frequent being the sub-serous variety. There were 5 cases of fibromata of the skin and 2 each of osteomata of the head and intracanalicular myxomata of the breast. There was but one case of adenoma of the breast; one dentigerous cyst of the lower jaw; one cyst of the neck (thyroglossal duct); one cyst of the anterior wall of the vagina, and one epulis.

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[1] The Prevalence of Cancer in the Philippine Islands, *Journ. Amer. Med. Ass.* (1908), **50**, 1663 to 1665.

Of the 28 cases of malignant growths there were 13 sarcomata, 12 carcinomata, and 3 of Hodgkin's disease. The sarcomata involved the scalp, testicle, femur, and dorsum of the foot twice; the forearm, eye, parotid, tibia, and skin once.

There were 6 cases of carcinoma of the stomach. The breast was carcinomatous in 2 cases, the pancreas, uterus, liver, and skin one each. The 3 cases of Hodgkin's disease all showed involvement of the supraclavicular and axillary glands.

PHILIP K. GILMAN.

REVIEW.

A Text-Book of the Principles of Animal Histology. By Ulric Dahlgren, M. S. and William A. Kepner, A. B. Cloth. Pp. xiii+515. Price, $3.75 net. New York: The Macmillan Company, 1908.

This work of more than 500 pages, containing nearly 500 illustrations of which about 300 are original, has had such a flattering reception and has been so favorably reviewed that it is unnecessary further to discuss its value. The authors state that the book "is intended to be a work that teaches general principles and teaches histology as a pure science and for its own sake. It is believed that it will serve as a broad foundation for future studies of morphology and embryology as well as for the medical studies." This object is well fulfilled. Rich fields heretofore untouched by any text-book, such as the tissues that produce electricity, light, gases, etc., are opened, offering the results of original research work on these subjects.

The illustrations are not only largely original, but they explain the text by their clearness and detail. Many of them are diagrammatic, thus furnishing an ideal method of instruction without sacrificing reality. In this way the structure of protoplasm is made plain, chromatin changes become distinct, the amplification of body surface is illustrated, the arrangements of muscles' cells is explained, the relation of absorptive surface is indicated, and many other obscure points are made clear. A bit of muscle fiber shows relaxation in the segment at one end and successive stages of contraction in all the other segments, and this is only one of many unusual illustrations.

The comprehensive character of the work is made clear by the following list of tissues, to each of which a chapter is devoted:

Epithelium.
Supporting and connecting tissues.
Tissues of motion.
Electric tissues.
Tissues of light production.
Tissues of heat production.
Circulatory tissues.
Nerve tissues.
Pigment tissues.
Alimentary tissues.
Ductless glands.
Tissues of respiration.
Gas-secreting tissues.
Excretory tissues.
Protective tissues.
Tissues of reproduction.
Nidamental and erectile tissues.
Nourishing membranes.

Improvement in style and in grammatical structure are to be desired and will doubtless be found in future editions of the work, of which it is to be hoped there will be many. If references are given they should be in greater number and form a complete bibliography. However, such a wide range of subjects is covered that an undertaking of this kind is scarcely feasible.

The book is not altogether suitable for beginners, but it is the best that I have seen and I most heartily recommend it to students preparing for medical work.

R. B. B.

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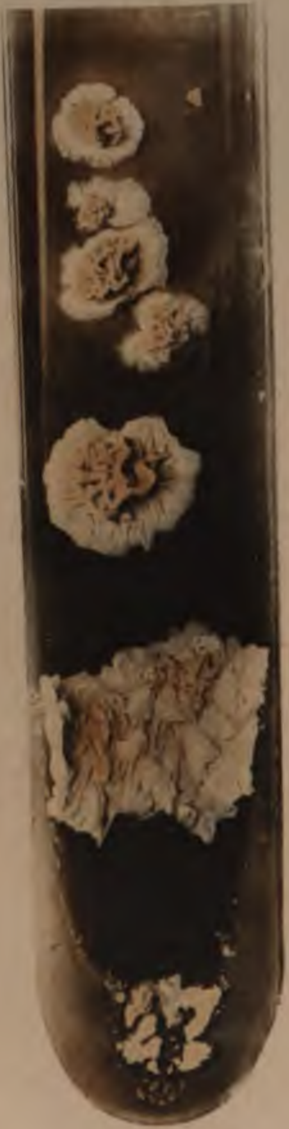

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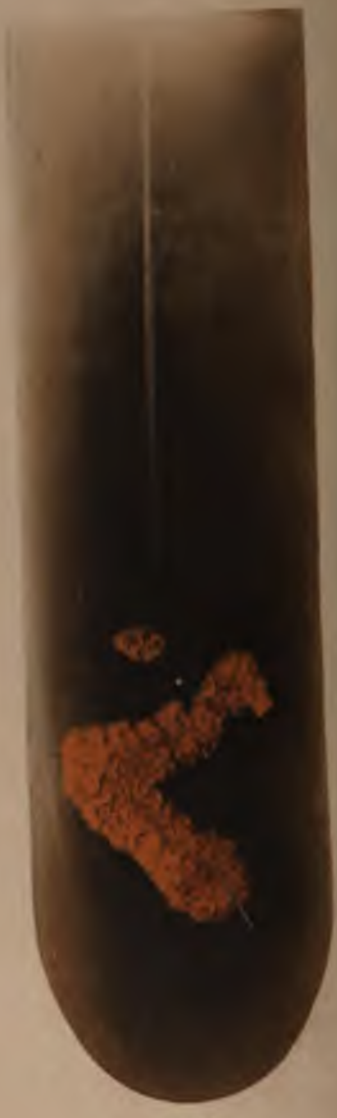

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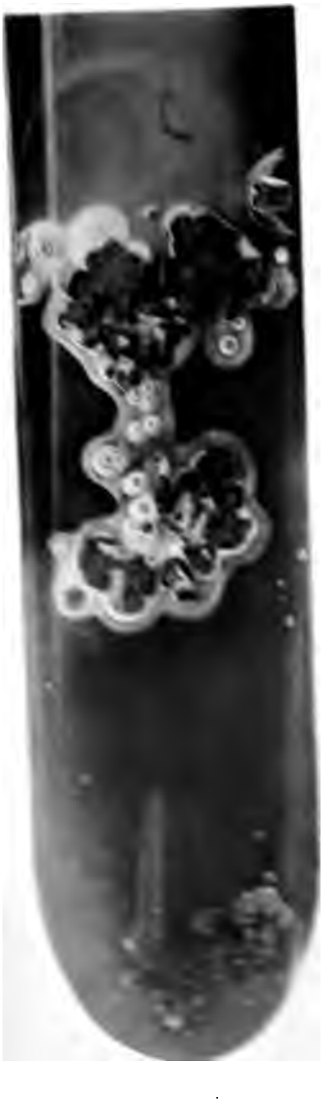

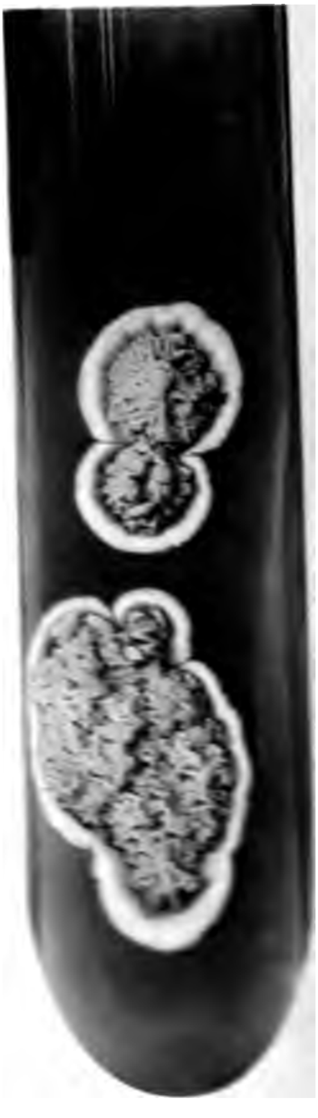

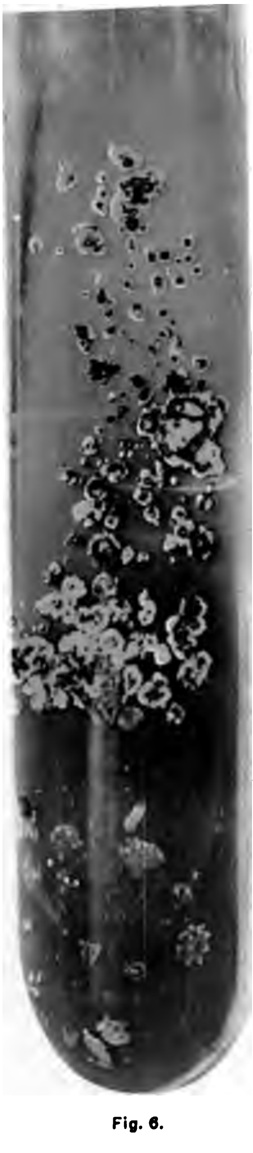

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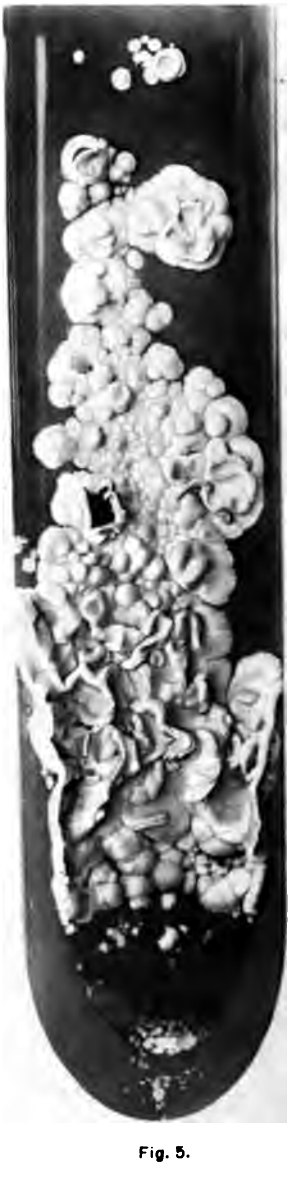

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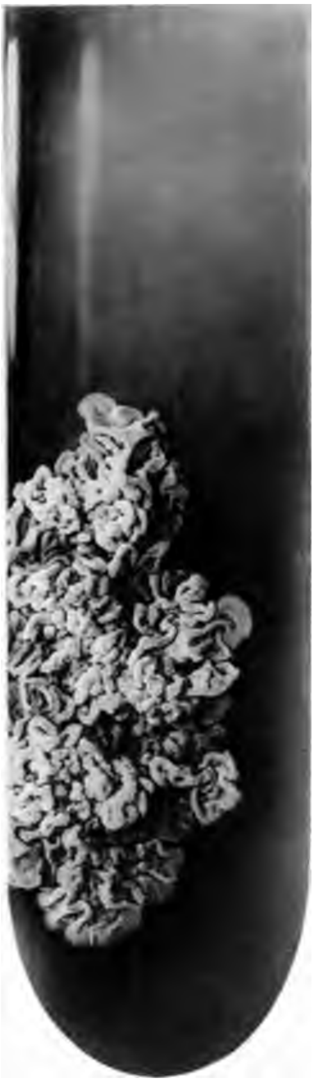

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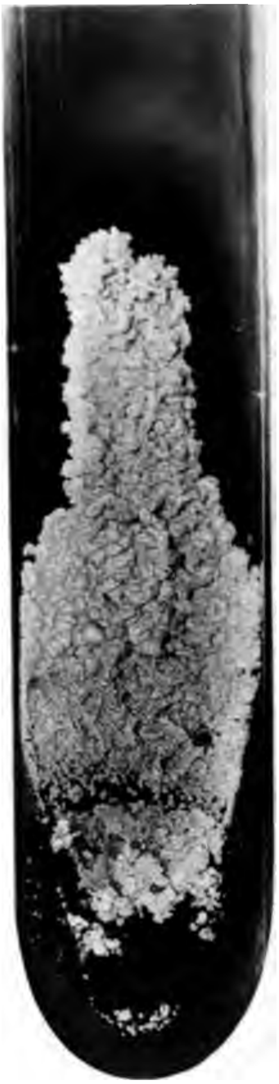

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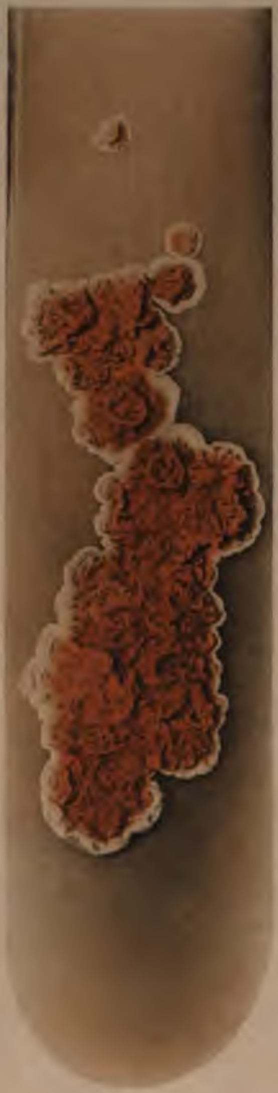

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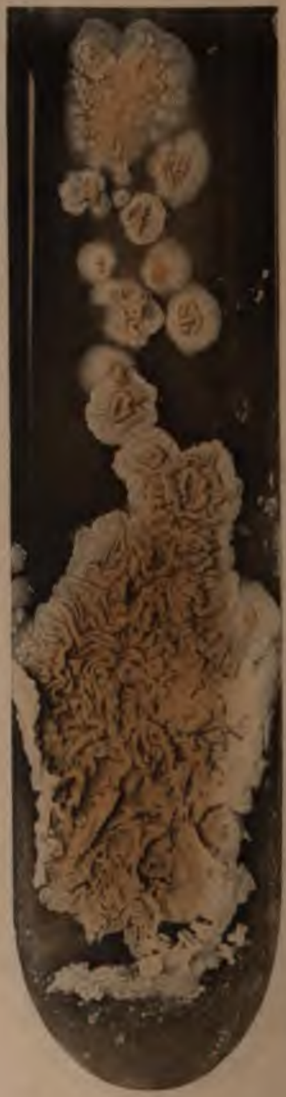

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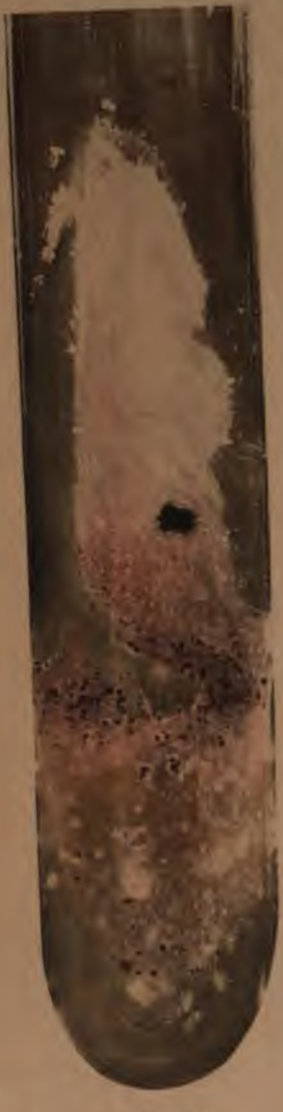

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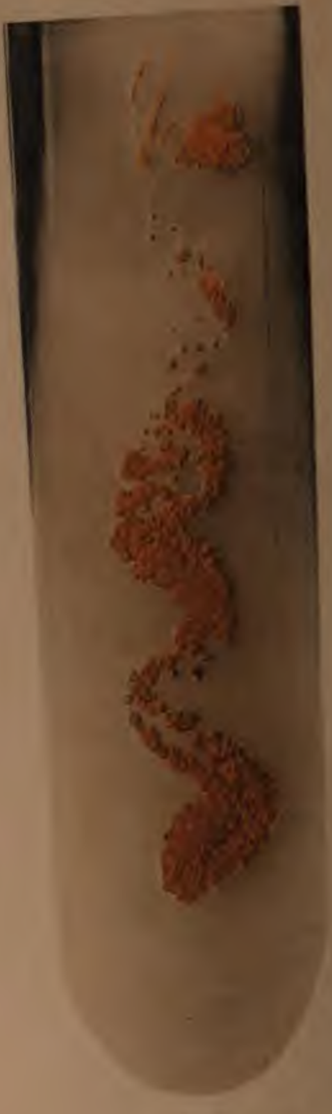

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[1] Out of print.

[2] The first four bulletins in the ornithological series were published by the Ethnological Survey under the title "Bulletins of the Philippine Museum." Later ornithological publications of the Government appeared as publications of the Bureau of Government Laboratories.

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[1] Out of print.

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